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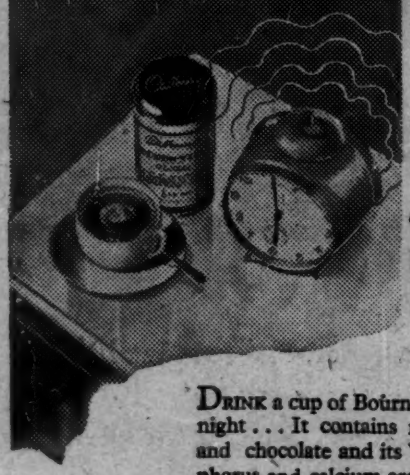

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 9 1944

TREATMENT OF HYPERTHYROIDISM WITH THIOURACIL

BY

A. M. NUSSEY, M.D., M.R.C.P.

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Until recently partial thyroidectomy was the treatment of choice for thyrotoxicosis. *X* rays and radium had their advocates, and some continued to pin their faith to iodine, either alone or in combination with various sedatives. It is true that in quite a number of mild cases of thyrotoxicosis the disease would abate spontaneously; but only too often, especially in severe instances, the patient treated medically for too long would become a physical, sometimes a mental, wreck, or fall an easy prey to intercurrent infection. The advent of thiourea, and especially of thiouracil, bids fair to alter the position radically. These preparations may represent only a milestone in the approach to a problem the real key to which may be a substance acting through the pituitary; but at present, to say the least, they offer a serious challenge to the hitherto undisputed sway of surgery in the treatment of hyperthyroidism. The use of thiourea and thiouracil in thyrotoxicosis is an example of how seemingly unrelated research may sometimes, almost by accident, be turned to advantage in treatment of disease. This research began when the Mackenzies and McCollum (1941), working on the effects of sulphaguanidine in rats, discovered that it had the property of inducing a hypothyroid state and enlargement of the thyroid gland in the experimental animals. At about the same time similar results were obtained by Richter and Clisby (1941, 1942), who used phenyl thiourea, and by Kennedy (1942), who used allyl thiourea which he isolated from rape seed. Later the Mackenzies (1943), and Astwood and his colleagues (1943), proved that, besides sulphaguanidine, other sulphonamide derivatives, and to a lesser degree sulphanilamide itself, also had the power to depress metabolism and cause hypertrophy of the thyroid gland in rats. In an endeavour to find a metabolic depressant suitable for clinical use these workers then tested a large number of compounds, and found that thiourea and thiouracil were the most effective and least toxic. These observations led to the first clinical trial by Astwood (1943).

The original workers and those who followed are all agreed that thiourea and thiouracil probably act by preventing the union of tyrosine and iodine into di-iodotyrosine, which is a precursor of thyroxine. Once thyroxine is present in the body thiourea and its derivatives cannot stop its action. This explains the lag observed in clinical response of thyrotoxicosis to thiourea and thiouracil, and is in keeping with the observation that desiccated thyroid gland is capable of counteracting the effects of these substances in experimental animals. Further light on the mode of action of thiourea is thrown by the paper of Campbell, Landgrebe, and Morgan (1944), who pointed out the great affinity of thiourea for iodine and have shown that thiourea given by mouth is quickly absorbed from the intestine, widely diffused through the tissue fluids, and very rapidly excreted unchanged in the urine. Williams and Bissell (1943), who successfully treated 9 cases of thyrotoxicosis with thiouracil, noted equally rapid absorption and excretion of this substance. They stated that blood analyses of 4 of their cases showed in each a fall of the protein-bound iodine to a normal or subnormal level. More recently Williams and his associates (1944a, 1944b) devised a method for the estimation of thiouracil in the blood, tissues, and urine, but whether such biochemical tests will prove a help in regulating the dose of the drug remains to be seen.

At present it is possible, when treating patients, inadvertently to exceed the optimum dose and to cause an increase in the size of the thyroid gland and a condition resembling myxoedema. The reason for these complications is presumably the same as that put forward by the experimental workers—namely, that when the supply of thyroxine falls below the needs of the body the pituitary gland is stimulated to excessive secretion of the thyrotrophic hormone, which in turn causes hyperplasia of the thyroid gland. This must have happened to the first patient described by Astwood (1943), to another given in detail by Himsworth (1943) in his first series of 6 cases treated with thiourea, and to several patients in the present series. Other complications known at present are granulopenia, thrombocytopenia, enlargement of lymph glands and spleen, fever, and skin eruptions, but these have been more frequently noted when thiourea was used (Newcomb and Deane, 1944; St. Johnston, 1944; and Astwood's first case, 1943). Now that the more palatable and less toxic thiouracil is freely available there is no reason why thiourea should be employed any longer. It is true that, using thiouracil, Gabrilove and Kert (1943) found that out of 9 cases they treated for thyrotoxicosis one developed fever, generalized enlargement of the lymph glands, and dermatitis, another fever and dermatitis, and a third moderate leucopenia, but their patients were all given rather heavy doses of the drug in addition to an unspecified quantity of barbiturates.

In a discussion on thiouracil at the Royal Society of Medicine, Himsworth (Himsworth *et al.*, 1944) drew a distinction between idiosyncrasy to the drug, which is liable to occur early, and toxic effects which follow prolonged overdosage. Under manifestations of idiosyncrasy he listed the complications mentioned above, and the toxic effects of overdosage he described as superficially resembling myxoedema. Of those taking part in the discussion Drs. H. P. Himsworth, E. P. Sharpey-Schafer, and H. Evans were favourably impressed with thiouracil. One of Himsworth's patients, who had rather large doses, died of agranulocytosis, and two of his other patients, whose goitres increased unduly as a result of the treatment, had to be operated on. Mr. C. Joll (Himsworth *et al.*, 1944), who used thiourea and thiouracil in 20 to 30 cases, presented results in 9, in which, in his opinion, the length of treatment justified making deductions. His failure to achieve success in 3 out of the 9 subjects was criticized at the discussion by Himsworth on the ground that in these iodine was used before thiouracil, and that the latter was not given a sufficiently long trial. Himsworth stated that he found no difference in response to thiouracil in either primary or secondary thyrotoxicosis. The cases mentioned in the discussion at the R.S.M. bring up the number of those fully reported to over 100.

It is obvious that further and more prolonged observations will be required before the treatment of thyrotoxicosis with

thiouracil can be placed on a more satisfactory basis. As a contribution to the problem a presentation is made of the data obtained from personal observations on 27 patients treated at Selly Oak Hospital for periods varying from a year down to 3 weeks. The results are summarized briefly in the accompanying table.

Discussion

The cases are classified into very severe, severe, moderate, and mild, partly on clinical grounds and partly on the basis of a routine preliminary B.M.R. estimation. The majority of patients had general enlargement of the thyroid gland, other had a nodular goitre, and both types responded to thiouracil equally well—a point already noted by Himsworth. In every instance except in Nos. 8 and 12 the initial treatment was administered while in hospital, thus making possible day-to-day observation of progress. Periods varying from 2 to 11 weeks passed before satisfactory clinical response was noted. The average stay in hospital was about 3 weeks. During this time no other drug, not even a simple sedative, was allowed. Where iodine was found to have been given, it was discontinued.

TABLE OF RESULTS

A	B	C	D	E	F	G	H	I	J	K
1	35 F	18 mths.	Moderate	+29%	23/10/43	23/11/43: +15 11/5/44: + 2 25/8/44: +11	—	23/11/43: 6,200, 71% 11/12/43: 7,600, 61% 8/1/44: 5,800, 69% 26/2/44: 5,200, 66% 1/11/44: 5,800, 71%	23 lb.	Initial treatment with thiourea tolerated badly. Transient rash when changed to thiouracil. At one time considerable swelling of neck, which disappeared on reducing the dose. Possible to omit treatment for 4 mths., but it had to be resumed a month ago
2	54 F	6 „	„	+27%	23/10/43	4/11/43: +19 17/11/43: + 5 3/2/44: +21 9/8/44: +10	—	26/11/43: 6,055, 55% 19/1/44: 7,200, 41% 1/2/44: 7,800, 51% 2/5/44: 6,200, 58% 1/11/44: 5,600, 74%	10 lb.	Given 53 g. of thiourea before change to thiouracil on 11/11/43. Tolerated both well. Now on 0·05 g. of thiouracil daily
3	40 F	12 „	„	+31%	25/10/43	8/11/43: +16 20/11/43: +12 3/5/44: +10	—	19/11/43: 9,600, 71% 4/10/44: 9,200, 70%	Nil	Had 25 g. of thiourea. Changed to thiouracil on 11/11/43. After end of Jan. did not attend till May, 1944, when there was no evidence of relapse. Now recurrence of mild features of thyrotoxicosis and 0·2 g. thiouracil resumed on 4/10/44
4	28 F	15 „	Severe	+45%	22/11/43	7/12/43: +26 12/1/44: + 8 19/6/44: +29	—	30/11/43: 5,000, 45% 10/1/44: 4,400, 62% 3/5/44: 4,200, 47% 8/7/44: 4,200, 47% 2/8/44: 3,600, 55%	6 lb.	Some days before treatment with thiouracil admitted with influenzal bronchopneumonia and given sulphathiazole. History of rheumatic mitral disease; her auricular fibrillation reverted to normal during treatment. At one time excessive increase in weight and enlargement of neck noted. This subsided when dose of thiouracil was reduced. Now on 0·05 g. daily
5	53 M	12 „	Very severe	+67%	23/11/43	6/12/43: +41 20/12/43: +18 17/1/44: +20	—	25/11/43: 5,600, 62% 7/12/43: 8,600, 75% 3/2/44: 4,600, 66% 17/3/44: 4,000, 58% 14/6/44: 5,200, 36% 6/9/44: 10,600, 59% 4/10/44: 5,600, 64% 1/11/44: 6,800, 57%	15 lb.	Temporary increase in size of goitre reversed by reduction in dose. Treatment omitted for 2 months, after drug given for 5 months, but had to be resumed now on 0·1 g. daily. Able to do housework
6	65 F	18 yrs.	Severe	+45%	25/11/43	13/12/43: +42	—	4/12/43: 6,200, 48%	1 lb.	Partial thyroidectomy 18 years before. In patient for 1 month. Died early in Jan. 1944, 3 weeks after leaving hospital
7	29 F	1 yr.	Mild	+19%	11/12/43	22/12/43: + 9 29/4/44: +25 7/7/44: +11	5,600; 79%	14/12/43: 6,300 13/1/44: 8,700, 75% 2/3/44: 7,600, 74% 19/6/44: 5,000, 53% 4/8/44: 7,000, 34%	Nil	Tachycardia was an outstanding feature, pulse of 100–120 per min. down to 80 after 8 months of treatment. Now on 0·05 g. thiouracil daily
8	40 F	18 mths.	Moderate	+30%	20/12/43	13/1/44: +28 7/2/44: + 2 21/6/44: Normal	7,600; 60%	10/1/44: 7,000, 84% 19/2/44: 10,000, 49% 17/4/44: 10,400, 59%	14 lb.	Partial thyroidectomy on 2/2/43, followed by recurrence of symptoms of thyrotoxicosis. Papular rash, chiefly on face, for 1 week, did not necessitate omitting treatment. Thiouracil stopped on 24/5/
9	40 F	1 yr.	Severe	+52%	6/1/44	25/1/44: +17 21/6/44: + 5	4,400; 45%	21/1/44: 6,200, 55% 1/2/44: 3,600, 48% 5/2/44: 4,800, 44% 14/6/44: 6,000, 52% 4/10/44: 4,700, 61%	22 lb.	Goitre increased for a time; went back to previous size on reducing the dose of thiouracil. No treatment since 4/10/
10	32 F	4 mths.	„	+67%	14/2/44	8/2/44: +63 2/3/44: +10 5/7/44: +12	6,200; 32%	9/2/44: 3,300, 42% 23/2/44: 4,200, 52% 2/3/44: 5,600, 51%	14 lb.	No treatment required since 5/7/44
11	21 F	3 „	„	+75%	1/3/44	16/3/44: +33 28/3/44: +22 13/4/44: − 7 25/7/44: +17	11,100	11/3/44: 14,200, 51%	6 lb.	At one time weight up by 23 lb.; neck much increased in size, and mild myxœdema. Relieved by adjusting dose of thiouracil. No treatment since 1/9/44
12	49 F	Over 5 yrs.	Moderate	+36%	5/3/44	17/10/44: +13	—	20/3/44: 6,800, 58% 30/8/44: 7,500	4 lb.	Congestive heart failure and auricular fibrillation dealt with first, before the initial B.M.R. and thiouracil treatment. Thiouracil omitted 2/8/44
13	23 F	2 mths.	Severe	+63%	16/3/44	20/5/44: +10	7,600; 47%	17/4/44: 6,000, 53% 5/7/44: 11,000, 48% 7/9/44: 12,000, 52%	8 lb.	No treatment required since 5/9/44
14	43 F	6 „	Moderate	+38%	30/3/44	14/4/44: +26 30/4/44: +18 17/8/44: + 7	9,069	18/4/44: 7,600, 54% 17/6/44: 7,300, 45% 4/8/44: 5,000, 65% 30/8/44: 4,000 13/10/44: 6,600, 71%	4 lb.	Tachycardia of 100 per min. persists. Now on 0·1 g. of thiouracil daily
15	27 F	2 „	Mild	+23%	8/4/44	20/5/44: +10	6,200; 47%	18/4/44: 8,800, 51% 14/6/44: 10,800, 59%	Nil	Had a partial thyroidectomy in 1[illegible]. Treatment omitted 5/9/44
16	72 F	8 yrs.	„	+21%	8/5/44	22/5/44: + 7	5,200; 45%	19/5/44: 4,000, 38% 7/9/44: 3,800, 33% 4/10/44: 3,800, 36%	7 lb.	Thyrotoxicosis of long standing. B.M.R. known to have been +54 in 1[illegible]. Treatment omitted 4/10/44
17	52 F	15 „	Severe	+35%	25/5/44	7/6/44: +27 26/6/44: + 7	7,000; 70%	6/6/44: 3,300, 69% 13/6/44: 4,600, 71% 4/8/44: 4,800, 71% 1/11/44: 7,600, 68%	11 lb.	Had radium treatment in 1934. Moderate tachycardia persists. Now on 0·1 g. thiouracil daily
18	52 F	18 mths.	Very severe	+71%	16/6/44	3/7/44: +78 24/7/44: +65 7/9/44: +58 4/10/44: +34	6,200; 46%	28/6/44: 6,400, 54% 24/7/44: 5,000, 59% 9/8/44: 5,600, 59% 8/9/44: 5,900, 44% 20/9/44: 5,900, 48% 1/11/44: 5,600, 55%	28 lb.	Rather resistant to treatment. In all was an in-patient for 11 weeks. Auricular fibrillation which was present restored to normal rhythm with quinidine. Now on 0·1 g. thiouracil daily
19	40 M	2 yrs.	Moderate	+39%	18/6/44	12/7/44: +17 25/10/44: − 7	6,700; 44%	29/6/44: 9,000, 68% 30/8/44: 6,900 12/10/44: 5,800, 67%	12 lb.	Frequent extrasystoles before treatment, almost disappeared after it. Now on 0·05 g. thiouracil daily
20	26 F	6 mths.	Mild	+23%	26/6/44	17/7/44: +14	8,000; 57%	12/7/44: 7,800, 54% 4/10/44: 9,000, 69%	6 lb.	Transient irritating papular rash; appeared on reducing dose of thiouracil. Now on 0·05 g. daily

TABLE OF RESULTS (*continued*)

A	B	C	D	E	F	G	H	I	J	K
21	52 F	2 yrs.	Severe	+47%	10/7/44	28/7/44: +22 18/8/44: +14	3,400; 47%	24/7/44: 5,000, 57% 9/8/44: 5,400, 53% 20/9/44: 4,600, 61% 1/11/44: 6,800, 71%	7 lb.	Auricular fibrillation, which was present, reverted to normal rhythm while under treatment with thiouracil. Now on 0·1 g. daily
22	45 F	9 mths.	,,	+29%	14/7/44	3/8/44: +26 19/9/44: + 9	4,400; 61%	1/8/44: 4,500, 44% 6/9/44: 6,900 4/10/44: 5,800, 38%	4½ lb.	Case judged to be severe on clinical grounds. Irritation of skin on arms and legs. Later slight eczematous eruption confined to hands. Now on 0·05 g. of thiouracil daily
23	42 F	? 7 yrs.	,,	+48%	1/8/44	10/8/44: +16	2,800; 56%	15/8/44: 4,700, 38% 7/9/44: 5,500, 68%	6 lb.	W.B.C. rose with treatment. Now on 0·1 g. of thiouracil daily
24	22 F	2 mths.	Moderate	+41%	14/8/44	30/8/44: + 7	4,800; 58%	26/8/44: 6,400, 49%	17 lb.	Treatment omitted 1/11/44
25	21 F	2 ,,	,,	+36%	4/9/44	28/9/44: +21 27/10/44: +12	7,600; 72%	26/9/44: 7,700, 62% 27/10/44: 6,200, 53%	6 lb.	Now on 0·2 g. of thiouracil daily
26	45 F	2 ,,	Severe	+50%	2/10/44	19/10/44: +17	3,600; 40%	10/10/44: 5,200, 38% 20/10/44: 5,000, 51%	8 lb.	Rapid clinical response to thiouracil. Now on 0·2 g. daily. Rise in W.B.C. with treatment
27	29 F	4 ,,	,,	+64%	13/10/44	28/10/44: +24	6,600; 40%	24/10/44: 7,800, 48%	8½ lb.	Able to leave hospital after a fortnight, much improved. Now on 0·2 g. thiouracil b.d.

Key to Table.—A: Case number. B: Age and sex. C: Duration of illness. D: Degree of thyrotoxicosis. E: % of B.M.R. above normal. F: Date of starting treatment with thiouracil. G: Later B.M.R. readings. H: Initial total white cell count and % of polymorphs. I: Later white cell counts and % of polymorphs. J: Gain in weight. K: Remarks.

for at least a month before thiouracil was administered. With the exception of Nos. 3, 6, and 18, who were seriously ill at the beginning of their treatment, strict confinement to bed was not practised.

During the initial in-patient phase the dose of thiouracil was generally 0.2 g. t.d.s. Three early cases also had thiourea in doses of 1 g. t.d.s. before thiouracil became available. Thus No. 2 received 52 g. of the substance and No. 3 had 35 g. No. 1, after only 7 g. of thiourea, developed toxic symptoms resembling those described by St. Johnston (1944), including extensive skin eruption, vomiting, headache, and fever. She was subsequently given thiouracil, when a much milder maculo-papular rash appeared on the parts of the skin exposed to light. The rash disappeared after the dose was reduced, and eventually she did exceptionally well. Skin rashes were caused by thiouracil in a few other instances. No. 8 had a papular eruption on the face, lasting one week, which cleared up of its own accord without having to modify the treatment. No. 20 had a transient papular rash which disappeared after the dose of thiouracil was reduced. No. 22 complained of occasional itching of the limbs, at first without any actual skin changes; later the parts exposed to light showed a scaly erythematous eruption, and it was interesting to note that as soon as she began to wear stockings the skin of the legs cleared rapidly, while the lesions of the hands and wrists disappeared much more slowly with a reduction in the dose of thiouracil. Only in No. 22 was there a moderate degree of leucopenia while the rash was present.

Signs of improvement were usually apparent 10 to 14 days after starting treatment. Severe thyrotoxicosis frequently responded to thiouracil as quickly as the moderate type, but in some of the former—e.g., Nos. 5, 17, and 18—one sometimes had to persevere for several weeks before the patients began to show a change for the better. Restlessness was usually the first to go, and then the flushed and moist skin would become paler and drier. The staring expression and the shiny appearance of the eyes, which are such striking features of thyrotoxicosis, would fade, the weight would begin to go up, and the tremor of the fingers would become less. Then the vascularity of the thyroid would diminish, as shown by lessening or disappearance of the bruit over the gland; and finally the tachycardia would subside. Oddly enough, it was in the milder cases—e.g., Nos. 7 and 14—that tachycardia tended to persist longest. In every instance, with the exception of No. 6, the patient would admit to feeling better after a few weeks' treatment, and all those gainfully employed previous to their illness were back at work long before it would have been possible had they had a partial thyroidectomy. Reduction of the B.M.R. was roughly parallel in each case with signs of clinical improvement. In nearly all patients the B.M.R. came down to within normal limits. Only in Nos. 6 and 19 has this not been achieved. In No. 6 the period available for treatment was probably too short, while in No. 19 it is almost certainly a matter of time before a normal basal metabolic rate is reached. Exophthalmos, which was present in only a few of the patients, was not appreciably influenced by treatment; neither did enlargement of the thyroid diminish to any extent. Four instances of auricular fibrillation were noted, two of which—Nos. 4 and 21—reverted to normal rhythm spontaneously in the course of the treatment, and another—No. 18—in whom this was achieved by means of quinidine. In the fourth—No. 12—auricular fibrillation persists, and owing to the fact that it is probably of at least 5 years' standing no attempt at conversion to normal rhythm with quinidine was made. The gain in weight was negligible in a few, appreciable in the majority, and in two it amounted to almost 2 st. since starting treatment. Only No. 3 lost weight. Excessive gain was sometimes accompanied by a bloated appearance, listlessness, and an increase in size of the thyroid gland. In contrast to the view held by Himsworth, I could see no difference at all between these manifestations and mild myxoedema. By a suitable reduction of the dose of the drug it was possible rapidly to reverse the pathological depression of metabolism, the excessive increase in weight, and the enlargement of the neck. The size of the neck was recorded in each case and checked at regular intervals, this proving an additional guide to the dose of thiouracil required. In fact, experience showed that the maintenance dose on which the pulse rate and general condition remained satisfactory varied from individual to individual, thus proving the value of periodic inspection. All patients were seen regularly after discharge—first at 2, then at 3, and finally at 4 weeks' intervals. There was only one patient—No. 3—who did not co-operate satisfactorily. She turned up only twice after discharge from hospital and ceased taking thiouracil of her own accord after 3 months. She was seen again in May, 1944, when her condition was found to have remained satisfactory and the B.M.R. was +10. More recently this patient came up again with symptoms of a slight recurrence of thyrotoxicosis, and her treatment was resumed.

As for the maintenance dose, the patients were usually given 0.2 g. of thiouracil, b.d., for 2 to 4 weeks after leaving hospital. Later, most of them were maintained on 0.2 g. and some on 0.1 or 0.05 g. daily. In a few instances it was found possible to omit treatment altogether—e.g., in No. 8 since May 24, 1944, No. 10 since July 5, 1944, No. 12 since Aug. 2, 1944, No. 13 since Sept. 5, 1944, No. 15 since Sept. 5, 1944, and No. 16 since Oct. 24, 1944. In No. 5, treatment had to be resumed because the man began to lose ground once more, and the same had to be done in No. 1 after omitting treatment for 3 months. Astwood (1943) mentions a patient in whom, after a relatively short period of treatment, he omitted thiouracil for a few weeks and had to resume it because of a recurrence of symptoms. Himsworth (1944) reported that in 3 mild cases he was able to leave off thiouracil for periods of from 7 weeks to 7 months.

Observations on the white cell count proved interesting. With the exception of Nos. 1–6 and 12, a preliminary count was always made before treatment was started, and low initial readings were not at all infrequent. These, although sometimes bordering on frank leucopenia, were not taken to be a bar to giving thiouracil, and surprisingly in those the white cell count usually showed a rise as the treatment proceeded. In no case was there an alarming fall of the white cell or polymorph count. Consistently low figures were seen only in Nos. 4 and 16. In this connexion it is worth noting the findings of

Goldsmith and associates (1944), that when liver extract is given to rats simultaneously with thiourea it protected them from neutropenia.

Three patients had operations of partial thyroidectomy before they came under the present review. No. 6, operated on 18 years before, had a nodular goitre, and a recurrence of symptoms 9 years after operation. About 12 months before coming to hospital she became short of breath, experienced nausea and vomiting, and when admitted her heart showed marked enlargement to the left and a systolic murmur at the apex. She showed no appreciable response after 4 weeks' treatment, and, unfortunately, although she was urged to stay, insisted on going home. It was reported later that she had died suddenly 3 weeks after leaving hospital. In No. 8, in which partial thyroidectomy failed to cure the condition, 5 months' treatment with thiouracil appeared to complete what surgery had left undone. Another milder recurrence, 8 years after partial thyroidectomy—No. 15—did equally well. No. 17, radium treatment of which 10 years before had been a complete failure, responded satisfactorily to thiouracil.

Conclusion

We have now in thiouracil a potent weapon for overcoming thyrotoxicosis. The drug, although not entirely devoid of risks, is much safer than operation. All patients suffering from thyrotoxicosis should therefore be given thiouracil. At some future date it may be possible to assess the initial and maintenance dosages on a more scientific basis, but at present, in the light of experience, a satisfactory working rule is to give 0.2 g. of thiouracil thrice daily for the first 3 to 5 weeks, after which the dose should be gradually reduced, and kept at the lowest possible level compatible with the patient's well-being. Slow response to treatment calls for patience, and not for increasing the dose beyond a safe limit. Leucopenia before the treatment should not be taken as a contraindication to the use of thiouracil. All patients treated with thiouracil should be kept under adequate supervision. Only more prolonged observations will tell whether thiouracil is capable of effecting a permanent cure within a measurable period.

Summary

A series of 27 unselected cases of thyrotoxicosis treated with thiouracil for periods varying from 3 weeks to 12 months are described.

Good response, with the exception of one long-standing instance, was noted in all.

The importance of continued supervision of the treatment is stressed.

It is submitted that the hitherto almost unrivalled surgical treatment of thyrotoxicosis may, in the light of further experience, have to give way to medical treatment.

Grateful thanks are due to both my medical and my surgical colleagues, who kindly passed on to me their patients with thyrotoxicosis, and thus made this series much larger than it would otherwise have been. Our biochemist, F. Morton, M.Sc., F.R.I.C., carried out the B.M.R. estimations, and Messrs. British Drug Houses generously supplied, free of charge, most of the thiouracil used in this investigation.

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M. J. MacNeal and M. C. Place (*Amer. J. Dis. Child.*, 1944, **68**, 30) record a case of fulminating meningococcaemia in a boy aged 8 years, who recovered after treatment first with sulphadiazine intravenously and later with the calcium salt of penicillin intravenously and intramuscularly.

THE HAEMOGLOBIN LEVEL IN MUNICIPAL SCHOOL CHILDREN

EFFECT OF IRON THERAPY, SCHOOL DINNERS, AND SEASON

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The lack of knowledge of normal haemoglobin levels in school children, of the physiological rise with age, and of the effects of iron therapy, diet, and economic circumstances has recently aroused attention in this country. The present paper represents an effort, only partially successful, to increase our knowledge of this subject.

Clinical Material

Children at two municipal schools were examined. One—school B—was in a London suburb, where 127 children, aged 7 to 12 years, were examined in Oct., 1942. Many of the pupils' fathers were black-coated workers in moderately comfortable circumstances. The other—school A—was in a small town near London where the children had repeated haemoglobin examinations during a period of over a year, beginning early in 1942. The number of children examined at this school was 325. Here economic standards were more varied, but very few families were below the poverty line, as shown by the supply of free milk or free dinners. About half the fathers were industrial or transport workers (mechanics, skilled craftsmen, unspecified munition workers, railway workers, etc.); about 23% were in the armed Forces, and another 13% were clerical workers or shop-assistants. About 43% of the mothers did paid work, part- or full-time, outside their own homes.

Technique, and Some Sources of Error

Estimations were made with a Haldane standard by the three of us, and figures are given with the National Physical Laboratory B.S.I. corrections applied for colour tube and pipettes. Apart from the percentage correction for the dilution tubes (a correction required because the distance between the 20 and 140 marks, and hence the diameter, differed from the B.S.I. standard), the mean N.P.L. correction for the tubes was −0.3 at 80%. This correction was obviously negligible, and was omitted. The maximum correction thus omitted on any one dilution tube was −0.9 at 80%. The blood was taken from a prick in the thumb after soaking the hand in hot water. The earliest estimations were made during a period of extremely cold weather in January and early February of 1942. The children at the time nearly all had chilled extremities, and in spite of soaking the hand in hot water, there were wide discrepancies in the results, presumably because of capillary changes and stasis. All readings taken during this period have been discarded as doubtful. It is probable that cold limbs, in spite of precautions to get a warm hand and a free flow of blood, produced inaccurate estimations at other periods, but it is difficult to see how this can be prevented under the conditions of field work. Another source of misleading results is, we believe, anxiety or apprehension on the part of the child: it was noticed that children showing anxiety often registered wide fluctuations in haemoglobin level.

Haemoglobin Level in Relation to Age and Sex

Table I shows that there was a fairly steady rise in haemoglobin level with age, though the numbers in the different subdivisions were not sufficient to even out chance fluctuations. Taking the mean haemoglobin level for the combined results at school A in Feb., 1942, and again in Feb. or March, 1943, together with school B in Oct., 1942, there was a rise from 87.8% at 7 years to 92.1% at 10 years—that is, a rise of 4.3 in three years, or an average rise of 1.4 per year of age, and each subdivision in Table I shows a rise with age of a similar order. The haemoglobin levels at school B were slightly

TABLE I.—*Changes in Haemoglobin Level with Age*

Age (years)	School A				School B		Schools A and B: 3 Previous Series Combined							
	Feb., 1942		Feb. or Mar., 1943		Oct., 1942		Boys and Girls				Boys		Girls	
	Mean Hb	No. of Children	Mean Hb	No. of Children	Mean Hb	No. of Children	Mean Hb	No. of Observ.	S.D.	Range	Mean Hb	No. of Observ.	Mean Hb	No. of Observ.
7	87·1	31	89·2	20	88·0	25	87·8	76	5·68	77–101	86·8	35	88·9	41
8	88·7	44	87·9	58	89·0	24	88·4	126	6·00	73–101	89·0	60	87·8	66
9	88·4	37	89·8	45	91·4	37	89·8	119	5·47	74–104	89·9	55	89·7	64
10	91·3	9	91·4	60	93·4	36	92·1	105	4·76	76–101	91·4	47	92·6	58
11	—	—	92·1	44	88·4	5	91·6	49	6·06	79–103	89·5	26	94·1	23
Total ..		121		227		127		475				223		252
Over 7 and under 11: Average of means ..	88·9		89·6		90·5		89·5				89·3		89·7	

higher than at school A, which may be a reflection of a slightly higher economic status.

The average of the mean Hb levels of boys and girls aged over 7 and under 11 (all figures in Table I combined) was 89.3 and 89.7% respectively—that is, the means for the sexes were all but the same. In the small group of 26 boys aged 11 the haemoglobin level (89.5%, S.D. 6.24) was lower than in girls of the same age (94.1%, S.D. 4.7) and also slightly lower than in girls or boys aged 10. However, the difference between the sexes at 11 years of age is not statistically significant, and the lower mean level of the boys' haemoglobin is probably quite fortuitous and due to inadequate numbers. So that, like other investigators (Osgood and Baker, 1935; Mugrage and Andresen, 1936), we have found no evidence of a difference in haemoglobin between the sexes at these ages.

Haemoglobin Level in Relation to Year and to Season

Children living in or near London and of similar economic class to those attending school A were examined by us in the second half of 1941 (Wills *et al.*, 1942). The average of the mean haemoglobin values for children aged 7, 8, 9, and 10 years respectively was in 1941 distinctly lower than that of the children of the same age examined in 1942 and 1943: the values were 83.4% in 1941, 88.9% in Feb., 1942, and 89.6% in Feb. and March, 1943. (The value for 1941 has been corrected so as to conform to the same standard as these later estimations.) Thus at school A in Feb., 1942, and a year later in Feb., 1943, the mean haemoglobin level of children of corresponding age differed little (Table I). There was, however, a rise of haemoglobin level with age during this period of 1942–3. The mean haemoglobin level of our control group, who received no medicinal iron, was 89.8% in Feb., 1942, and 91.1% in Feb. and March, 1943, when the average age had increased by a year (see Table II). This is a rise of 1.3, which is just about equivalent to the mean increase in haemoglobin level with each year of age shown in Table I. The year's increase in haemoglobin was not evenly spread over the year, but occurred between March and July. There was actually a fall in haemoglobin level between Feb. and March, 1942, a rise between March and July, 1942 (these changes being statistically significant), and thereafter no significant change up to the following Feb. and March, 1943.

TABLE II.—*Changes in Mean Haemoglobin Level during Year 1942–3 in a Group of Children at School A given No Iron*

Date of Examination	No. of Children	Mean Hb	Change in Hb since Previous Examination	Change in Hb since Feb., 1942
1942: Feb. ..	50	89·8 ± 0·68	—	—
March ..	80	87·5 ± 0·50	−2·3 ± 0·84*	−2·3
April–May ..	76	89·1 ± 0·56	+1·6 ± 0·75*	−0·7
July	79	91·7 ± 0·47	+2·6 ± 0·73*	+1·9
Nov. ..	67	91·4 ± 0·55	−0·3 ± 0·72	+1·6
1943: Feb.–March	73	91·1 ± 0·62	−0·3 ± 0·83	+1·3

* The change in haemoglobin level is more than twice the standard error of the difference; in July it is more than 3½ times the standard error of the difference.

Effect of Iron Therapy on Haemoglobin Level

Iron medication was given to about half the available children at school A from Feb. to July, 1942. The iron preparation used was fersolate (Glaxo), and each child in the iron group was ordered one pill daily, increasing in seven days to 4 pills daily for 5 days in the week, to be taken in the class-room with the school milk. Four pills provided 4 gr., or 260 mg., of iron (ferrous), 0.04 gr. of copper, and 0.04 gr. of manganese. Most children took their dose regularly. In a few cases it probably gave rise to some abdominal discomfort or looseness of stools and was consequently stopped, or sometimes it was stopped for quite irrelevant reasons.

The head master's allocation of children to classes in this school was determined by age, and the age groups were then subdivided according to ability. Thus nearly all the 11-year-olds would be in class 1A, 1B, or 1C—the brightest in class 1A and the least advanced in class 1C, and similarly for each age group.

The children were given iron medication by classes. For example, all children whose haemoglobin had been estimated in class 2A acted as controls; those in 2B and 2C received iron pills. In the next age group the allocation was reversed, and 3A children (the brightest of this age group) received the pills, and 3B and 3C acted as controls. It so happened that the children examined in the A divisions were often about equivalent in numbers to those in divisions B and C of the same age group. By this means it was hoped to prevent any possible confusion in iron administration and to keep the groups evenly balanced. Children on the iron list have been included in the tables as having iron irrespective of their absences from school (during which time iron medication ceased), as otherwise selection of both controls and iron cases would have been necessary. The effect of iron medication is shown in Table III. The children given fersolate showed an immediate rise in haemoglobin, which continued until July, when treatment was stopped, the mean total rise being 7.0%. The children not given iron showed a fall in haemoglobin till March, and then a rise; but measured from February the total rise of the control group was only 1.9% (Table II). However, as the initial haemoglobin level of the children given

TABLE III.—*Effect of Iron Medication on Mean Haemoglobin Level of Children at School A*

Date of Examination	Iron Group					Control Group		
	Iron Therapy	No. of Children	Mean Haemoglobin	Change in Hb since Previous Examination	Change in Hb since Feb., 1942	No. of Children	Mean Haemoglobin	Difference in Hb. Iron minus Control
1942: Feb.	Started	46	86·8 ± 0·96			50	89·8 ± 0·68	−3·0 ± 1·20*
March		69	89·0 ± 0·68	+2·2 ± 1·20	+2·2	80	87·5 ± 0·50	+1·5 ± 0·84
April–May ..		71	91·8 ± 0·58	+2·8 ± 0·89*	+5·0	76	89·1 ± 0·56	+2·7 ± 0·81*
July	Stopped	62	93·8 ± 0·66	+2·0 ± 0·88*	+7·0	79	91·7 ± 0·47	+2·1 ± 0·81*
Nov.		55	90·6 ± 0·56	−3·2 ± 0·87*	+3·8	67	91·4 ± 0·55	−0·8 ± 0·78
1943: Feb.–March ..		56	90·5 ± 0·67	−0·1 ± 0·87	+3·7	73	91·1 ± 0·62	−0·6 ± 0·91

* The difference in haemoglobin level in these groups is about 2½ to 3¾ times the standard error of the difference.

TABLE IV.—*Effect of Iron Medication on Mean Haemoglobin Level of Children at School A Examined in Feb. and also in March, 1942*

Date of Examination	Iron Group		Control Group	
	No. of Children	Mean Hb	No. of Children	Mean Hb
1942: Feb. ..	41	87·0	48	89·9
March ..		89·9		87·6

fersolate was lower than that of their controls, the difference in haemoglobin level between the controls and iron-treated cases in July was only 2.1%. Even so, the iron group had significantly higher haemoglobin values than the controls from March till July. In July iron medication was stopped, and by November the haemoglobin level of the iron cases had dropped and was within 1% of the mean for the controls but 3.8% above their own mean before iron medication was begun 9 months previously. The difference in the trend of haemoglobin values between iron cases and controls over this period is confirmed by examining subdivisions of the main groups, for in each age group in the iron series the mean haemoglobin value showed a rise between Feb. and March, 1942, whereas in each age group in the controls the mean haemoglobin fell over the same period; moreover, if the comparison is limited to children who supplied observations in both February and March (see Table IV) the result is practically the same as for the whole group shown in Table III. Hence we can safely assume that iron medication prevented a fall in haemoglobin and produced instead a fairly steady rise, continuing till medication was stopped in July, but that once medication was stopped there was a fall in haemoglobin to about the level of the controls.

Iron medication over this period of five months did not reduce the absentee rate. Between February and July (i.e., during two terms) the mean attendances of control cases and iron cases were almost identical; each child in the iron group averaged 237.9 attendances, while each child in the iron group averaged 237.3.

Effect of School Dinners on Haemoglobin Level

The effect of school dinners on haemoglobin level was investigated (see Table V). At school A the midday meal

TABLE V.—*Effect of School Dinners on Mean Haemoglobin Level of Children who had had School Dinners for Over 3 Months*

Age in Years	School A, Feb. or March, 1943				School B, October, 1942				Schools A and B Combined			
	Dinner Children		Controls		Dinner Children		Controls		Dinner Children		Controls	
	No.	Hb	No.	Hb	No.	Hb	No.	Hb	No.	Hb	No.	Hb
7	8	88·6	9	90·3	4	92·6	18	87·8	12	89·9	27	88·6
8	30	89·1	25	87·3	6	89·6	17	88·7	36	89·1	42	87·9
9	24	89·7	19	90·2	13	90·4	19	91·3	37	89·9	38	90·7
10	32	90·9	26	92·0	11	93·1	23	93·7	43	91·4	49	92·5
11	18	94·0	21	90·9	2	94·3	3	84·5	20	94·0	24	90·1
7–12	112	90·5	100	90·9	36	91·5	80	90·4	148	90·7	180	90·2

when first instituted was the so-called Oslo, or modified Oslo, meal, which proved unpopular. From June, 1942, an ordinary hot dinner was provided, usually consisting of meat and two vegetables and a sweet course. This at first was not quite adequate in quantity for the older children, but by the end of 1942 the calorie value seemed ample. A similar meal was provided at school B. Table V shows the mean haemoglobin level of children who had had school dinners of this type for not less than three calendar months, many for much longer periods. At school B, in 1942, the children having school dinners had a mean haemoglobin level approximately 1% higher than the controls; but this slight superiority was not constant in the subdivisions, and was presumably the result of chance. At school A the difference between the haemoglobin of "dinner children" and controls was less than 0.5%, the controls being slightly higher this time. Thus these figures provide no evidence that school dinners had any influence on haemoglobin level. The suggestion we previously made that school dinners caused a slight but significant rise in haemoglobin level in school A in the summer of 1942 (Mackay *et al.*, 1942) is not supported by the present findings.

Effect of Home Circumstances on Haemoglobin Level

It has already been stated that many of the children's mothers did paid work outside their homes. Of 235 mothers of children examined in Feb. or March, 1943, 57% were housewives working only in their own homes; about 28% did part-time and 15% did full-time work outside their own homes. Over a half of those earning wages were engaged in some form of paid domestic work. As one might expect, mothers were more likely to go out to work when their children were older; thus 10% of mothers of 7- and 8-year-old children, and 18% of mothers of 9- to 12-year-old children, did full-time paid work. In Table VI the mean haemoglobin levels of children

TABLE VI.—*Effect of Home Circumstances on Haemoglobin Level of Children examined at School A in Feb. or March, 1943*

	Mother's Occupation			Three or More Earners	No. of Non-earning Children in Household			
	Housewife Only	Part-time Earner	Full-time Earner	1–2 Children not Earning	1	2	3	4 or More
No. of children ..	134	65	36	18	73	87	47	19
Actual mean Hb ..	89·5	90·8	90·9	92·0	90·4	90·1	89·7	88·5
Expected Hb for age	89·8	90·4	90·4	90·3	90·0	89·8	90·4	90·2
Actual less expected Hb	−0·3	+0·4	+0·5	+1·7	+0·4	+0·3	−0·7	−1·7

are shown according to whether or not the mother went out to work. In each of the three subdivisions the mean haemoglobin level is within 0.5% of the expected figure according to age. Hence haemoglobin levels in this series of children were not affected by the mother working outside her home. We have no information as to the relative financial status of these three groups, but there is little doubt that economic causes play a large part in determining whether a mother shall go out to work and that paid work considerably enhances her means.

The next five groups shown in Table VI suggest that economic factors were influencing haemoglobin level, though, unfortunately, numbers are too small to provide proof. In these five groups the highest mean haemoglobin level was in households with three or more wage-earners and not more than two non-earning children, and the mean haemoglobin level of these children—namely, 92.0%—was 1.7% above the expected level for age. The lowest mean was in households with four or more non-earning children, and their mean haemoglobin level was 1.7% below the expected figure. The mean haemoglobin level of children in households with one, two, or three children was intermediate, and showed a progressive fall, the figures being 90.4, 90.1, 89.7, and 88.5%. It was thought that children of men in the Forces might, for economic reasons, have a lower haemoglobin level than the children of civilians, but the difference was negligible—only 0.4%: children of men in the Forces, 89.7%; children of civilians, 90.1%. Further investigations on the effect of home circumstances on the haemoglobin level were planned, but have fallen through for the time being owing to the evacuation of school-children.

Discussion

The children examined at school A in the present investigation were of similar economic status to the small group of school-children included in our 1941–2 investigation. We found a rise in mean haemoglobin level between the second half of 1941 and early in 1942, but little change between early 1942 and early 1943. On the other hand, our 1941 values are similar to Davidson's values for municipal-school children in Edinburgh in the next year—i.e., 1942—and he observed a rise between 1942 and 1943 (Davidson *et al.*, 1943). Our 1942 values for municipal-school children are nearly as high as Davidson's 1942 values for private-school children (Davidson *et al.*, 1943). The causes for the changes in haemoglobin level are probably to be found in the food available to the children. It seems probable that the haemoglobin levels of school-children were lowered by food shortages accentuated by uneven distribution in 1940–1. Possibly food supplies improved more quickly for the children examined by us, or perhaps, as they lived

in a small town with many gardens, there was more opportunity for augmenting their diet from home-grown produce than existed for the Edinburgh children, and this may have accounted for the higher levels in our group in 1942. The following official account of food available in the United Kingdom before our 1941 investigation is taken from *Food Consumption Levels in the United States, Canada, and the United Kingdom* (Combined Food Board Committee, 1944). "In the United Kingdom there was a sharp fall in food supplies in 1940 and 1941, particularly of meat, visible fats, sugar, and fruit, which greatly reduced the palatability as well as the nutritional value of the diet. . . . At the period of greatest shortage in the first half of 1941 calorie supplies fell to 2,680, animal protein to 33 g., and fat to 105 g. per head per day, and there were indications that the diet was inadequate." It is a curious fact that the haemoglobin of children showed little increment between the ages of 5 and 11 years in our earlier series (last six months of 1941) or in Davidson's 1942 series, yet in Feb., 1942, in Oct., 1942, and in Feb. and March, 1943, in our present investigation, there is a steady increase in haemoglobin with age. A possible explanation is that our earlier investigation included small batches of children in a number of different schools and immunization clinics in different seasons, and that the rise with age was masked in this more heterogeneous group. Whether the same holds for the Edinburgh children we do not know.

It is well known that school-children's rate of growth in height and weight is not even throughout the year. Widdowson and McCance (1944), for example, have recently demonstrated that boys at two public schools grew much more rapidly in height and weight in holidays than in term-time. Our figures suggest that the rise in haemoglobin level with age also shows fluctuations during the course of the year. The main increment in haemoglobin level in our series occurred between March and July. We have no evidence as to whether variations in the physiological rise in haemoglobin level were directly due to seasonal differences in the incidence of droplet or other infections, or were associated with changes in the diet, or were dependent on a variety of factors. Vitamin C has been thought to influence the absorption or utilization of iron, and a sharp summer rise in the level of blood ascorbic acid has been demonstrated in this country during the war years, the rise occurring as a result of the consumption of new potatoes. This change in ascorbic acid intake, however, could not account for the rise in haemoglobin level, as the increase in haemoglobin occurred too early in the year.

Though the group of children given iron at school A had haemoglobin levels only 2.8% lower than Davidson's private-school children, iron medication produced a mean rise of 7% in 1942. Iron produced a rise within a month and at a time when the haemoglobin level of controls was falling, but in the spring and summer the haemoglobin level of controls also rose, and the difference in level between treated cases and controls in July, 1942, before medication was stopped, was only 2.1. Though this small difference in level was statistically significant, the absentee rate of controls and treated cases did not differ. With so small a difference in haemoglobin level perhaps an increased resistance to infection in the treated group could scarcely be expected in this period. The superiority of the treated cases in haemoglobin level was not maintained after treatment was stopped. A similar rise in the haemoglobin level of Edinburgh municipal-school children given iron therapy was shown by Davidson and Donaldson in 1944.

There is at present little or no evidence to show whether or not children having dinners in school commonly get in addition a large share in their own rations at home. If they do, their diet should, of course, be better than that of children who have only their home rations and no school dinners. Our investigation shows no improvement in haemoglobin level as a result of school dinners, though children in better economic circumstances may have somewhat higher haemoglobin levels even under our system of rationing (Wills and Bingham, not yet published).

The fact that a mean rise of 7% was produced in the group receiving iron medication and that the haemoglobin level in our municipal-school children was lower than that of children of higher economic status certainly suggests that there were many children in our group with subnormal levels, but does not establish what the normal level should be. A few children had persistently high haemoglobin levels; for example, a boy aged 9 years who received no iron treatment had the following values in the course of a year: 100.7, 101.1, 100.0, 97.9, 100.0, 101.1, and 99.1. But such a case was an exception; most children, even those with several consecutive high readings, showed fluctuations in the course of a year. Some fluctuations were no doubt due to errors in technique, others to illness of the child, but it is probable that physiological changes due to exercise, differences in temperature, and emotion also caused fluctuations.

Summary

The haemoglobin levels of children at two municipal schools were estimated with the Haldane haemoglobinometer. At school B 127 children were examined in Oct., 1942; at school A haemoglobin estimations were repeated at intervals for over a year in 1942–3, and 325 children in all were examined. The mean haemoglobin level at 7 years was about 88%, and there was an increase with age to approximately 92% at 10 years. The mean haemoglobin level for each age was approximately the same in Feb., 1942, as in Feb. or March, 1943. The age increment for this twelve-months period occurred between March and July, after a drop in haemoglobin level between February and March. Iron therapy for five months in 1942 produced a mean rise of 7.0%, but when treatment was stopped the haemoglobin fell to approximately the level of the controls. Dinners provided in school had no effect on the haemoglobin level. Children who had eaten a midday dinner in school for three months and upwards had a mean haemoglobin level within 0.5% of controls who had no school dinners. Results suggest that in families where there are three or more children not earning wages the haemoglobin levels are likely to be lower than the average, but numbers were too small to be more than suggestive. The haemoglobin levels in 1942 and in 1943 were higher than they were in the latter half of 1941 for children of similar economic status examined by us.

Our sincere thanks are due to the medical officers of health and their staffs for their help. The head masters and their teaching staffs assisted us most generously in spite of all the extra work thrown upon them, and we are glad to express our gratitude. We are much indebted to Dr. W. J. Martin for certain statistical analyses.

[POSTSCRIPT.—Since this paper was written there has appeared in the *Journal* (1944, **2**, 333) an interesting paper by Davidson and his co-workers on haemoglobin levels in 1944 as compared with 1942 and 1943. In this two-year period they found a mean rise in haemoglobin of about 4½% at one municipal school in Edinburgh and about 13% at another. Allowing (as found by us) for a rise with age of 2.8% in two years, this means an increment of about 2% and 10% respectively between 1942 and 1944. We, on the other hand, found a rise at an earlier date; children examined early in 1942 had a haemoglobin level 5½% higher than similar children examined in the second half of 1941, and between 1942 and 1943 we found little change. The Edinburgh workers conclude that the compulsory use in bread of 85% extraction flour and a consequent increase in iron intake "has been the chief factor responsible for the raised haemoglobin levels." The use of flour of 85% extraction was made compulsory all over Great Britain from March 23, 1942, and very little such flour was used anywhere in the country before that date; hence this cannot have been responsible for the rise in haemoglobin observed by us by Feb., 1942. Moreover, the use of this flour had little, if any, effect on the haemoglobin level in our group between Feb., 1942, and Feb. and March, 1943, since the levels at these dates differed by only 0.7%. Their haemoglobin level was, however, responsive to iron, for iron given in large doses produced a rise of 7%. The addition of calcium carbonate to the national bread was started gradually from April, 1942, so presumably much of the bread consumed by the children under our observation between April, 1942, and Feb. and March, 1943, contained this addition. Our observation therefore makes us hesitate to accept the view that the rise in haemoglobin level observed in Edinburgh school-children was attributable to changes in the composition of bread, although, like Prof. Davidson, we feel certain it was due to an improvement in the diet.]

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THE DIETARY CONTROL OF ALLOXAN DIABETES IN RATS

BY

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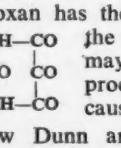
The importance of fat in lessening the severity of diabetes has long been known, but still receives little emphasis. Recently it has been underlined by observations in dogs made diabetic by the daily injection of anterior pituitary extracts. Marks and Young (1939) have found that when these dogs are given a diet which is almost exclusively fat the glycosuria and the ketonuria are greatly diminished. It seems as if on a fat diet the metabolism of these dogs ceases to be abnormal. Recently we have studied the production of diabetes in rats by the injection of alloxan, and have taken the opportunity to observe the effect of dietary changes, in particular of a high-fat diet, upon the glycosuria so produced. Our first experiments showed that the abrupt substitution of a high-fat diet for a normal diet caused a disappearance of glycosuria which was accompanied by some ketonuria. Although this ketonuria was transitory, we endeavoured to avoid it altogether by introducing fat in the diet in stages. In our first attempt to do this we used an unpalatable diet, and the results served only to demonstrate that a reduced calorie intake reduces glycosuria. In other experiments we successfully demonstrated the inhibitory effect of fat on glycosuria when the calorie intake was maintained.

Alloxan has the formula shown, and is closely related to the purines chemically. It is a substance which may arise in the natural course of metabolic processes in the body, and may be one actual cause of diabetes in man.



Shaw Dunn and McLetchie (1943) produced permanent glycosuria in rats by injecting a succession of doses of varying size at varying intervals. Working in April, we observed that two doses given subcutaneously on two successive days, each 16 mg./100 g., produced glycosuria in 8 rats of about 200 g. weight. In two of these the glycosuria disappeared after 4 days, but in 6 rats it persisted. Alloxan seems to be inactive by mouth; for, in 3 rats, four times the above dose on four successive days, followed by eight times the dose on two days, did not cause glycosuria.

Effect of Diet on Glycosuria

In the accompanying Chart is shown the onset of glycosuria in two rats which were kept in the same cage. On the 2nd day, after the injection of the second dose of alloxan, the dextrose excretion rose to 5 g. in 24 hours, and on the 7th day to 7.7 g. The average excretion for the first 13 days was 5.5 g. in 24 hours. During this time the rats received a mixed diet, the composition of which was as follows: 19% ground wheat, 19% bran, 19% oats, 9% ground maize, 9% ground barley, 5% fish meal, 10% meat and bone meal (this being 50% protein), 10% skimmed-milk powder, plus yeast, cod-liver oil, and salt; the calorie value was estimated to be 3.8 cals. per gramme. On the 13th day the diet was changed to a high-fat diet of 90% margarine and 10% casein, plus a salt mixture. As the Chart shows, the glycosuria dropped to 0.5 g. on the first day and disappeared thereafter. In two other pairs of rats the same prompt disappearance of glycosuria was seen on changing from the normal diet to one consisting of 20% casein and 80% margarine. In one pair the dextrose excretion on the normal diet rose during 9 days to 10.9 g. per 24 hours, the mean figure being 7.0 g. On the high-fat diet it fell at once to 0.3 g., 0.2 g., and 0.2 g. on three successive days. On restoration of the normal diet it rose again to a mean figure of 7.6 g. for the next four days. In another pair of rats the normal diet was given for 30 days before it was changed, to observe whether any spontaneous arrest of glycosuria occurred. The mean dextrose excretion was 3.5 g. daily during this period, and showed no sign of declining. When the diet was changed to a high-fat diet, glycosuria disappeared in the first 24 hours and, save for traces on four occasions, remained absent for 6 weeks, until the rats were again given the normal diet. These observations show clearly that the substitution of a high-fat diet for a normal diet abolishes the glycosuria in rats as found by Marks and Young in the dog.

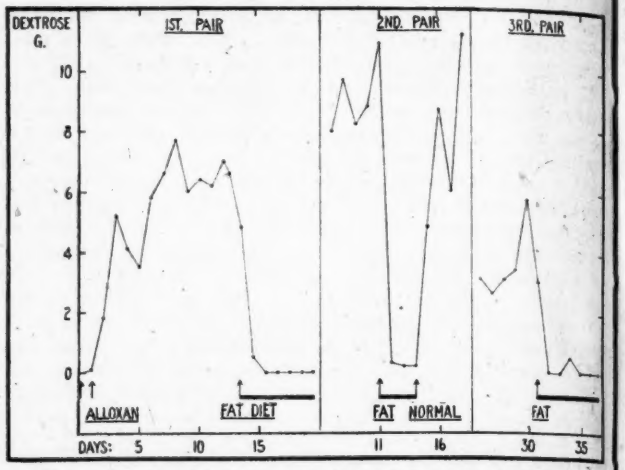


Chart showing the daily excretion of dextrose (ordinate) in the urine of three pairs of rats. In the first pair the onset of glycosuria is shown after two injections of alloxan. On the 13th day a high-fat diet was given. In the second pair the effect of 3 days of high-fat diet is shown. In the third pair the effect of high-fat diet is shown after 31 days of normal diet. The high-fat diet abolished the glycosuria in all three pairs.

Fat Diet and Ketonuria

The sudden change to a high-fat diet produced ketonuria in varying degree, as shown in Table I. The ketonuria was determined by the gravimetric method of van Slyke (1917). Table I shows that the ketonuria in the rats given 90% of fat reached the high figure of 132 mg. on the 3rd day, thereafter declining; it was, however, much less in the two pairs which were given 80% fat.

TABLE I.—*Ketonuria on High-fat Diet. (Mg. Acetone per Day.)*

Rats	Fat in Diet	Days of Fat Diet				
		1	2	3	4	5
1st pair	90%	2	12	132	49	24
2nd ,, ...	80%	2	9	4	—	—
3rd ,, ...	80%	0	6	15	0	0

Gradual Change to Fat Diet.—The rat is an animal which develops ketonuria less readily than man, and, indeed, outside the spring months can eat a diet wholly fat for a week or more with little or no ketonuria (Burn and Ling, 1928). An attempt was therefore made to introduce fat in the diet gradually in order to avoid the occurrence of ketonuria: if ketonuria could not be avoided in the rat it certainly could not be avoided in man.

Importance of Total Calorie Intake

The first experiments were made by changing from the normal diet to a diet of casein, margarine, starch, and a salt mixture. The proportion of casein was kept constant at 20%, while the proportions of carbohydrate and fat were altered. A diet of any one composition was continued for a period of not less than 5 days, for which the food consumed was measured and the calorie value calculated. The results in a pair of rats are given in Table II. In the column headed "Diet" the letter S indicates the diet of casein, margarine, and starch, as distinct from N, the normal diet. The figure following S is the percentage of fat in the diet. For each period the mean daily calorie intake and the mean daily dextrose excretion are recorded, and, finally, the body weight of the two rats at the end of each period is shown.

At first, with a diet containing only 40% of fat, the food intake was reasonably good and the dextrose excretion high. On raising the fat percentage to 60 the dextrose excretion dropped very low, but coincidently with this change the rats ate much less food and the calorie intake fell to little more than half. That the main cause of the diminution of glycosuria was the drop in calories rather than the increased fat was shown by the fact that when the fat percentage was decreased

TABLE II

Diet	No. of Days	Mean Daily Calories	Mean Daily Dextrose Excretion (g.)	Body Weight at End (g.)
S. 40	8	143	3·0	364
S. 60	8	80	0·2	333
S. 50	5	82	0·02	308
S. 40	5	70	0·2	293
S. 30	8	92	0·1	253
N	11	152	2·2	373
N	12	190	5·85	420
N	6	75	0·6	342

in stages to 50, 40, and 30% glycosuria remained very slight. The low calorie intake was reflected in a serious fall in body weight, for at the end of the fifth period the rats had together lost more than 100 g. They were then given the normal diet, 40 g. per day. They ate all of this, and dextrose excretion rose to a mean figure of 2.2 g. In the next period the normal diet was increased, and the calorie intake rose to 190; as a result the dextrose excretion more than doubled. At the end of this period the body weight was fully restored. A final demonstration of the importance of calorie intake on the amount of dextrose excreted in the urine was provided by reducing the diet to 20 g. per day. The dextrose excretion again fell to a low figure.

Effect of Fat on Dextrose Excretion

The attempt to demonstrate the importance of fat had so far failed because the mixture of casein, starch, and margarine was not liked by the rats, and they ate very little. In another pair of rats the experiment was performed by adding fat to the normal diet. The result is shown in Table III. During

TABLE III

Diet	No. of Days	Mean Daily Calories	Mean Daily Dextrose Excretion (g.)	Body Weight at End (g.)
S. 20	6	68	0·3	378
N	6	202	4·9	443
N. 20	6	212	4·0	450
N. 30	6	203	2·8	495
N. 40	6	188	2·3	493
N. 50	10	172	1·0	503
N. 60	16	157	0·3	500
N. 70	6	165	Nil	488

the first period the rats were eating the unpalatable mixture and were then given the normal diet (N). Although the diet was of approximately the same composition the calorie intake rose to about three times the previous value, the body weight increased, and the dextrose excretion rose from 0.3 to 4.9 g. per day. Margarine was then incorporated in the normal diet —first 20%, then 30%, until, finally, 70% was included.

As the percentage of fat rose the mean daily excretion of dextrose steadily fell. With 60% of added margarine the dextrose was as little as 0.3 g. per day, and with 70% the urine became completely sugar-free. While this occurred the calorie intake fell only a little. On the normal diet without added fat the calorie intake was 202 per day at a time when the dextrose excretion was 4.9 g. When the diet contained 70% added fat the calorie intake was 165—that is to say, about 80% of the previous intake—and since 5 g. dextrose, representing 20 calories, was no longer lost in the urine, the calorie usage was 90% of that on the normal diet. The maintenance of the calorie intake was reflected in the maintenance of the body weight, which remained near 490 g. on the diets containing 30, 40, 50, 60, and 70% of added fat. After each change in the diet the urine was examined for acetone bodies on three or more successive days. Ketonuria occurred on only one day of the whole period, which was approximately 8 weeks. It amounted to 19 mg. acetone, and occurred after the rats had been given 50% of added fat. Strangely enough, there was no ketonuria when the added fat amounted to 60 or 70%. Thus in this experiment glycosuria was abolished by a high-fat diet which did not reduce the calorie intake sufficiently to affect the body weight.

Permanence of the Diabetes

When these diabetic rats were given alternate periods of a normal diet and a high-fat diet it was found that the glycosuria recorded when they were eating the normal diet gradually diminished in successive periods. Figures illustrating this change in one pair of rats are given in Table IV. It is

TABLE IV

Period when Diet Normal	Mean Dextrose Excretion in 24 Hours (g.)
2nd–13th day	5·5
33rd–42nd ,,	4·4
105th–127th ,,	2·3
161st–171st ,,	1·6

The first day was the day on which glycosuria first appeared.

uncertain at present whether this decrease in dextrose excretion was due to intervening periods of high-fat diet or not. Perhaps diabetes produced in rats by alloxan diminishes in course of time even on a normal diet. Further work is in progress to determine whether a high-fat diet not only prevents glycosuria but also restores functional islet tissue in rats.

Discussion

These experiments show how convenient a tool alloxan is for the study of diabetes in groups of animals. Most experimental studies hitherto made have been carried out in dogs or in cats, made diabetic either by removal of the pancreas or by Young's method of repeated injections of anterior pituitary extract, which has the great advantage that the pancreas remains. Even so, the production of diabetes takes a considerable time and requires much anterior-lobe material. Two injections of alloxan are enough to produce diabetes in the rat, so that diabetes can be studied in groups of animals with ease. We have been able to demonstrate that glycosuria is eliminated by diets of high-fat content. Allen (1917) recommended high-fat diets for the treatment of human diabetes, as did Newburgh and Marsh (1920), and Petrén (1925) later. Haist, Campbell, and Best (1940) from their studies of the insulin content of the pancreas conclude that fasting, fat-feeding, and the injection of insulin are three factors which allow the pancreatic islets to rest. As already stated, Marks and Young (1939) found that a diet of beef suet diminished both glycosuria and ketonuria in dogs made diabetic by anterior lobe extracts, and Dohan and Lukens (1939) have confirmed this. A diet exclusively fat could not, of course, be given indefinitely. While we have not found it possible to make a sudden transition to a high-fat diet without increasing ketonuria, we have found that by a gradual increase in the fat content of the diet it is possible to abolish glycosuria without producing ketonuria and at the same time to provide a diet containing enough calories to maintain body weight reasonably well. Thus we have been able to demonstrate that alloxan diabetes in the rat can be brought under complete control by diet.

The difficulty in applying these results to man is that most people do not believe that man (in particular, a diabetic patient) can eat a high-fat diet without developing ketonuria and exposing himself to the risk of coma. Our knowledge of the mechanism of ketonuria is still small. Petrén (1925) stated that a diet of butter diminished acidosis, whereas a protein diet increased it. Marks and Young (1939) also say: "The results of our investigations have shown that the ketonuria is at a maximum when a meat diet is given, and is lowest with the prolonged feeding of fat." It seems clear that further progress in the dietary control of human diabetes must await a clearer understanding of ketonuria.

Summary

Rats have been made diabetic by the injection of alloxan. When a high-fat diet was substituted for the normal diet the glycosuria disappeared and remained absent until the normal diet was resumed. This abrupt change to a high-fat diet was accompanied by some

ketonuria. When the fat in the diet was increased gradually, glycosuria disappeared without the appearance of ketonuria (except on one day in 8 weeks). The amount of diet eaten containing 70% of added fat provided 90% of the calories available in the amount of normal diet eaten, and maintained body weight.

After successive periods of high-fat diet the glycosuria seen on return to the normal diet steadily diminished.

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ANTIBACTERIAL ACTION OF 2-AMINOPHENOL (*O*-AMINOPHENOL)

BY

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In the course of work with a compound between cholic acid and sulphanilamide we discovered that some intermediate substances devoid of sulphanilic groups had a greater activity against Gram-negative bacilli than the final compound. This led to the investigation of a series of compounds for their activity against this group of organisms. Although the investigation is still in progress this paper records the results obtained with 2-aminophenol, as they appear to warrant its trial as a local antiseptic.

The use of sulphonamides and penicillin has brought to light the need for adequate chemotherapeutic treatment of infections due to or kept up by such organisms as *Proteus* and *Ps. pyocyanea*. Acridine derivatives are perhaps the most effective in this respect, although these compounds are toxic to leucocytes and tissue cells. McIntosh and Selbie (1944) recommend a powder consisting of 1 part proflavine and 99 parts sulphathiazole, and claim that it affords protection against pyogenic cocci, clostridia, and Gram-negative bacilli. Recently a group of compounds classified as synthetic detergents have been recommended for local antisepsis. Their action *in vitro* was described by Baker *et al.* (1941), who showed that the cationic detergents had a significant effect on Gram-negative bacilli, although this was less pronounced than their action on Gram-positive organisms. Two of this group—C.T.A.B. and phemeride—have received a clinical trial. The action of C.T.A.B. has been studied by Barnes (1942) and Williams *et al.* (1943, 1944), but unfortunately its antibacterial action is drastically reduced by the presence of organic matter. Phemeride has been shown by Iland (1944) to have an antibacterial action stronger than that of C.T.A.B., to be effective in the presence of 50% blood, and to be relatively non-toxic to the tissues of the body. Unfortunately both these compounds are very much less active against Gram-negative bacilli than against the pyogenic cocci. For the treatment of *Ps. pyocyanea* infections Berry (1944) and Gough *et al.* (1944) have recommended ethylene glycol monophenyl ether (phenoxetol), which, although a rather feeble antibacterial agent, appears to be particularly active against this organism.

Experimental

In the following experiments proflavine (2 : 8-diaminoacridine sulphate) has been tested in parallel with 2-aminophenol in order that a comparative picture can be obtained. 2-aminophenol is readily soluble in water. Fresh aqueous solutions have a pale-brown colour which deepens on standing, and after a time a slight precipitate forms. In spite of this well-known instability to oxygen and light there is no appreciable difference in bacteriostatic activity between fresh and 7-day-old solutions.

Bacteriostatic Action in Broth.—Serial dilutions were made in broth and then a suitable inoculum of the organism to be tested was added to each tube. Most of the tests were carried out in broth at *p*H 7.5 containing 1% "lab-lemco," 1% peptone (B.D.H.), 0.5% NaCl, and 0.005% *p*-aminobenzoic acid. Variation of media, however, did not materially affect the results. Table I shows the

TABLE I.—*Bacteriostatic Action in Broth at 37° C. (Size of Inoculum less than 500 Organisms in Each Case)*

Organism	Limiting Dilution of Chemical causing Complete Inhibition of Growth			
	2-aminophenol		Proflavine	
	1 Day	7 Days	1 Day	7 Days
Bact. typhosum ..	32,000	16,000	64,000	64,000
Proteus vulgaris ..	32,000	32,000	64,000	64,000
Ps. pyocyanea ..	8,000	4,000	8,000	4,000
Staph. aureus	64,000	32,000	64,000	64,000
Str. pyogenes	64,000	64,000	500,000	500,000

bacteriostatic activity of 2-aminophenol and proflavine obtained with various bacteria when a small inoculum of less than 500 viable organisms was used. Some variation in results occurred in different experiments with 2-aminophenol; the figures given represent an average. The activity of proflavine was rather more constant.

Table II shows the results obtained with *Staph. aureus* when inocula of 3.4 million, 34,000, and 340 viable organisms respectively

TABLE II.—*Effect on Antistaphylococcal Action of Varying Size of Inoculum*

Size of Inoculum of Staph. aureus	Limiting Dilution of Chemical causing Complete Inhibition of Growth			
	2-aminophenol		Proflavine	
	1 Day	7 Days	1 Day	7 Days
340 viable organisms	128,000	32,000	128,000	64,000
34,000 ,, ,,	32,000	32,000	64,000	64,000
3·4 mill. ,, ,,	4,000	4,000	64,000	32,000

were used. As will be seen, 2-aminophenol is very much less active against a large inoculum than against a small one, whereas the activity of proflavine is not so greatly affected by the number of organisms.

Bactericidal Tests.—Suspensions of organisms in 2-aminophenol and proflavine respectively were made, such that the final concentration of chemical was 1 : 1000 and the number of organisms per ml. about 20 millions. The tubes were left at room temperature, and viable counts were made after 6 hours and 24 hours. In a typical experiment with *Bact. typhosum* the original concentration of organisms was 17.5 millions per ml. After 6 hours 5.5 millions

TABLE III.—*Effect of 2-aminophenol and Proflavine on Str. pyogenes in Human Blood in Slide Cells*

	Fresh Defibrinated Blood							Blood in 1 : 1000 Liquoid			
	2-aminophenol										
Dilution of chemical:	1/4000	1/8000	1/16,000	1/32,000	1/64,000	1/128,000	None	1/16,000	1/32,000	1/64,000	None
No. of colonies of streptococci ..	0	0	0	0	2	2	2	0	0	32	28
	Proflavine										
Dilution of chemical:	1/100,000	1/200,000	1/400,000	1/800,000	1/1·6 mill.	1/3·2 mill.	None	1/100,000	1/200,000	1/400,000	None
No. of colonies of streptococci ..	0	0	1	1	2	2	2	0	30	35	28

per ml. had survived in 2-aminophenol and only 300 in proflavine. After 24 hours both compounds had killed all the organisms. In a control tube consisting of a similar suspension of organisms in water slight multiplication occurred.

Antibacterial Action in Blood in Slide Cells.—As Fleming (1930–1) has shown, most of the antibacterial agents used before the discovery of sulphanilamide destroy leucocytic function in dilutions which have no effect on bacterial growth. Many bacteriostatic compounds are also inactivated by blood or serum. The following experiment was carried out to determine whether either of these statements applied to 2-aminophenol. Two series were set up in parallel; in one case fresh defibrinated blood was used, and in the other blood 1:1000 liquoid. It was assumed that 1:1000 liquoid would destroy all leucocytes. Serial dilutions of 2-aminophenol and proflavine were made in isotonic saline, mixed with equal quantities of blood, and a suitable inoculum of streptococci added. Controls consisting of saline, blood, and organisms only were included. The mixtures were transferred to slide cells, which were sealed and incubated for 24 hours. Table III gives a typical result with a small inoculum of *Str. pyogenes* consisting of approximately 30 viable organisms per slide cell. These figures show that 2-aminophenol has a considerable antibacterial activity in the presence of 50% blood, and the compound does not interfere appreciably with phagocytosis in greater dilutions than it is bacteriostatic.

Action of 2-aminophenol on Penicillin.—The effects of mixtures of penicillin and 2-aminophenol on *Staph. aureus* were studied. A large inoculum of staphylococci will grow in a concentration of 1:8000 2-aminophenol, although much greater dilutions are inhibitory to smaller inocula. Serial dilutions of penicillin were made in plain broth and in broth containing a final concentration of 1:10,000 and 1:100,000 2-aminophenol. An inoculum of approximately 4 million staphylococci was then added to each tube. The results are shown in Table IV. It will be seen that even a dilution of 1:100,000 2-aminophenol increases the antibacterial activity of penicillin.

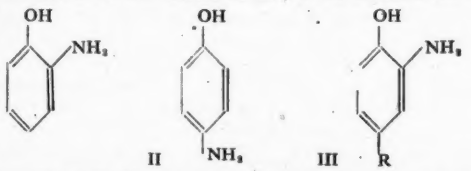
TABLE IV.—*Effect of Penicillin + 2-aminophenol on Staph. aureus when an Inoculum of Approximately 4 Million Organisms was used*

Penicillin, Units per ml. (approx.)	Plain Broth	1 : 100,000 2-aminophenol in Broth	1 : 10,000 2-aminophenol in Broth
None	++	++	+ → ++
1/4	0	0	0
1/8	0	0	0
1/16	0	0	0
1/32	0	0	0
1/64	++	0	0
1/128	++	+	0
1/256	++	++	0
1/512	++	++	0
1/1000	++	++	0

Plus signs indicate degree of growth as observed by turbidity. 0 = No growth.

Toxicity.—(1) *Skin sensitivity:*—This was tested on 6 human volunteers. A 1:500 solution of 2-aminophenol in water was rubbed into the same area of skin every day for a week. No reactions of any kind were observed and no irritation was felt. (2) *In mice:*—A series of 18 mice were given varying doses of 1% solutions of 2-aminophenol and proflavine respectively by subcutaneous injection. Doses of 0.4 g. 2-aminophenol per kg. of body weight were tolerated, but 0.5 g. or more per kg. was fatal. Proflavine was fatal in doses of 0.2 g. per kg.

Activity of Allied Compounds.—The antibacterial activity of 2- and 4-aminophenol (I, II) suggested a further investigation designed to determine the effects of molecular substitution in these



I II III

substances. The following compounds were therefore prepared and tested for antibacterial activity: 2- and 3-methyl-4-aminophenol, 5-methyl-2-isopropyl-4-aminophenol (6-aminothymol), 2-methoxy-4-aminophenol (5-aminoguaiacol), 2-aminoanisole (*o*-anisidine), N-acetyl-2-aminophenol, 3-, 4-, 5-, and 6-methyl-2-aminophenol, 4-carboxy-2-aminophenol and its methyl-, ethyl-, and *iso*-propyl esters, 4-phenyl-2-aminophenol, and 4-nitro-2-aminophenol (sodium salt, B.D.H.).

As a result of this work the conclusions reached were: (I) The 4-amino- (*p*-amino-) phenols (II) are generally so unstable that their use as therapeutic agents would be seriously limited. Work on them was not pursued, although 4-aminophenol as well as 2- and 3-methyl-4-aminophenol showed antibacterial activity of the order of that of 2-aminophenol itself. The remaining substituted 4-aminophenols were inactive. (I) Activity among the substituted 2-amino- (o-amino-) phenols (I) was limited almost entirely to substances of the class (III), but was absent where R was $-COOH$, $-COOCH_3$, $-COOC_2H_5$, $-COOCH(CH_3)_2$, or $-NO_2$. The most active substituted 2-aminophenol was 4-methyl-2-aminophenol (3-amino-*p*-cresol, III; R = $-CH_3$), and the activity of this substance was of the same order as that of 2-aminophenol itself.

So far we have not discovered a substance in which substitution has enhanced the activity of 2- or 4-aminophenol. Compounds of formula III, however, should be worth further investigation, and this is being undertaken.

Discussion

The mode of action on becteria of 2-aminophenol is not known. Like the sulphonamides, the compound is mainly bacteriostatic in action, and is very much more effective *in vitro* against a small number of bacteria than it is against a large number. 2-aminophenol in strong solutions, however, is slowly bactericidal. 4-aminophenol (*p*-aminophenol) has been shown by Bernheim *et al.* (1937) to have a considerable effect on tissue oxidations. These workers found that this compound, compared with a large number of similar substances, was the most active in inhibiting the oxygen uptake of liver suspensions.

Williams (1938, 1943) has studied the fate of 2-, 3-, and 4-aminophenol in the body. He has shown that 2-aminophenol when fed to rabbits by stomach-tube is excreted in conjugation with both sulphuric acid and glucuronic acid. No free aminophenol was excreted. He gave 1-g. doses of 2-aminophenol to 6 rabbits of 2.5 kg., apparently without toxic effect. He also showed (Williams, 1943) that 2- and 4-aminophenol glucuronides were methaemoglobin-formers *in vitro*.

Further observations on this group of compounds are required, but its low toxicity and its bacteriostatic activity against the Gram-negative bacilli suggest that 2-aminophenol may be of value as a local antiseptic.

We are glad to acknowledge the help of J. D. Oriel, of Guy's Hospital Medical School, in the preparation of substituted aminophenols.

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MEDIASTINAL TERATOMA SUCCESSFULLY REMOVED BY OPERATION

BY

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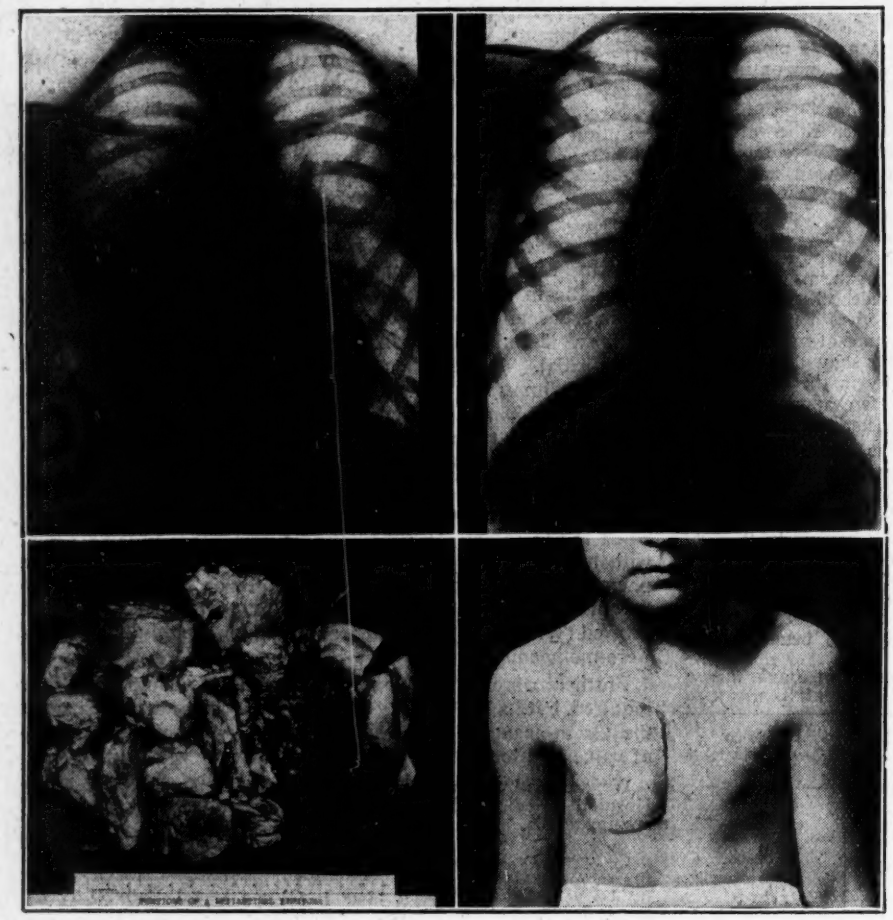
The following rare case is of interest, being that of a teratoma in a child aged 7 which was successfully removed.

Case History

In Jan., 1944, the patient was referred to me by Prof. E. J. Wayne and Dr. Thompson. The history was somewhat scanty, but the child had complained of shortness of breath while playing and on going uphill, and the mother, wondering if her heart was at fault, brought her to the Children's Hospital, Sheffield. Examination of the chest showed that the cardiac area of dullness was considerably increased to the right, and a radiograph disclosed that there was a tumour which occupied a large part of the right hemithorax. Further investigation revealed that it was roughly oval and lying in the anterior mediastinum. Scrutiny of the film showed that the shadow was not of homogeneous consistency, but was an irregular fine one which was very suggestive of bone. A diagnosis of mediastinal teratoma was made. The child was transferred to the Royal Infirmary, Sheffield, and was about to be operated upon when she developed scarlet fever and had to be sent to the local fever hospital.

She was readmitted on March 13, and the operation took place on March 21. The anaesthetic was ether–oxygen administered by an Oxford vaporizer. The chest was opened by an incision running parallel to the second rib, then down the margin of the sternum

and outwards along the sixth rib. The costal cartilages were cut on the bevel to prevent overlapping when the chest was closed. The right pleural sac was stripped away and a window raised of



chest wall. This revealed a large yellowish-white tumour, which was found to be relatively free on blunt dissection below, but was more firmly attached towards the upper pole. Owing to its large size it would have been necessary to enlarge the opening in the chest; so, to overcome this difficulty, the tumour was reduced in bulk by removing a series of wedges of tissue until it had reached reasonable proportions. It was finally removed by further digital dissection. As the upper pole seemed to be the most likely place for a blood supply, since none had been encountered, a clamp was placed across the last piece of tissue which held the tumour. To avoid infection the window in the chest was closed without drainage and the air aspirated out of the cavity to prevent surgical emphysema. Sero-sanious fluid collected during the next few days, which was aspirated on one occasion, but, as is so common in all chest operations, could not find any fluid on a subsequent attempt. The fragments of tumour when collected were found to weigh 12 oz.

My colleague, Dr. L. C. D. Hermitage, undertook the examination of the specimen and his report is as follows:

"Sections from various parts of the tumour show the structure of a multipotential teratoma. The following structures are present: (1) fatty areolar tissue; (2) cartilage; (3) ossifying cartilage; (4) bone marrow; (5) thymus gland tissue complete with epithelial pearls; (6) branching tubules lined by semi-stratified ciliated epithelium with plain muscle, cartilage, and numerous glands in the walls suggestive of bronchial epithelium; (7) tubular collections of melanin pigment; (8) cystic spaces lined by cubical epithelium forming papillary processes, the nature of which is not clear: they resemble the pink-celled cyst of the breast; (9) areas of connective tissue containing calcospherites."

The child made an uninterrupted recovery and was discharged on April 6.

A radiograph taken three months after operation showed a perfectly normal chest. There appeared to be a tendency to form keloid in the scar, so *x*-ray therapy was instituted.

In a review by Lloyd Rusby (1944) of dermoid cysts and teratomata of the mediastinum based on a study of the world's literature, it is stated that only some 245 cases, exclusive of six original cases, had been published between 1827 and 1939.

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Medical Memoranda

The Incomplete Antibody in Rh Immunization

The recognition of an Rh antibody which combines with homologous red cells *in vitro* but does not agglutinate them was announced independently in June of this year by Wiener and by one of us.

The "blocking" antibody (Wiener, 1944) or "incomplete" antibody (Race, 1944) is specific for one part of the antigen complex of Rh-positive cells. If this antibody could agglutinate, it would be of the type which has been variously called anti-Rh standard, anti-Rh 85%, anti-Rh_0, Δ, and rho. It reacts with the antigen common to the genes Rh_1, Rh_2, Rh_0, and the rare Rh_z. However, the complexities of antigenic components, genes, antibodies, and nomenclatures need not be gone into here.

Wiener has pointed out that this "blocking" antibody can be detected in some cases in which immunization is suspected and the mother or recipient is Rh-negative, but in which no antibody can be found by the ordinary means. The purpose of this note is to draw attention to this latest method of detecting immunization of an Rh-negative person and particularly to Wiener's technique, which is more sensitive than that described by Race. The following is Wiener's description of the test.

"The technique of the test is simple. First, one drop of a 2% suspension of Rh-positive cells and a drop of the patient's serum are mixed in a small test-tube and allowed to react in a water bath at 38° C. for 30 to 60 minutes. Then a drop of a suitable dilution of an active anti-Rh serum is added, and after an additional incubation period of 30 to 60 minutes the reactions are read. If blocking antibodies are present no agglutination will occur, or the clumping will be markedly weakened."

The example given of a suitable dilution of an anti-Rh serum is 1 : 5, when the original titre was 60.

We have tried Wiener's technique on a number of sera collected from Rh-negative women over about two years and stored at minus 20° C. Whereas Wiener placed the tubes in a water bath we used an incubator at 37° C., re-suspending the sedimented cells when adding the active anti-Rh serum after the first period of incubation. Of 19 cases in which the history sounded typical of haemolytic disease and yet in which no anti-Rh had been detected the incomplete antibody was found in 6. Of 26 cases in which a trace of anti-Rh had been detected the incomplete antibody was found in 19.

These results confirm the importance of testing for the presence of the incomplete antibody in any serum from a Rh-negative woman in which no anti-Rh can be found. The less sensitive the technique for detecting anti-Rh agglutinin the more useful will be the test for the incomplete antibody. In some cases it will yield the only evidence of immunization and in others will strengthen that given by the finding of only a trace of agglutinin.

A fairly extensive search involving more than 100 mothers with histories suggesting haemolytic disease has failed to give any evidence of incomplete forms of the other three types of anti-Rh agglutinins.

R. R. RACE, M.R.C.S., L.R.C.P.
G. L. TAYLOR, M.D., PH.D.

Cambridge.

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Reviews

EXPERIMENTAL BASIS FOR NEUROTIC BEHAVIOUR

Experimental Basis for Neurotic Behavior. Origin and Development of Artificially Produced Disturbances of Behavior in Dogs. By W. Horsley Gantt, M.D., Associate in Psychiatry and Head of the Pavlovian Laboratory, Johns Hopkins University. (Pp. 211. $4.50.) New York and London: Paul B. Hoeber, Inc.

The full title of this volume conveys almost as much as can be put into a brief review. The book deals very largely with observations on one dog, "Nick," which was under observation for 12 years and has been in a state of nervous imbalance for a decade. Considerable additions have been made to the original observations of the Pavlov school, particularly in the study of aberrations of sexual function. The author claims that, in animals, the origin and spread of nervous imbalance can be detected before it is properly expressed, can be traced in its development, and followed as it extends to the various physiological systems. Social and personal relationships can also be studied.

The book is stimulating and conveys a challenge, and probably marks the beginning of an epoch of productive work in this important field. For, as the author rightly points out, "in such a periodically recurring chaotic world state of affairs any approach to the question of emotional imbalance is important." Although the most detailed observations have been made on one animal, Dr. Horsley Gantt lays special stress on the fact that individual variations are very great. We feel irresistibly drawn to his conclusion that there is in these experiments much that is applicable to the problems of tortured mankind. We congratulate the author on a work full of interest.

DRUGS AND THEIR ACTIONS

A Concise Pharmacology and Therapeutics of the More Important Drugs, together with an Introduction to the Art of Prescribing. By F. G. Hobart, Ph.C., and G. Melton, M.D., M.R.C.P. Second edition. (Pp. 168. 12s. 6d.) London: Leonard Hill, Ltd. 1944.

The title of this book is misleading, for pharmacology is an experimental science, which is not expounded by giving a list of drugs and saying a little about the action of each. While it is a useful work for the doctor in practice who wants a book of reference handier than the *Extra Pharmacopoeia*, yet because it is called "Pharmacology" it is unlikely to be bought by the qualified man, and its main sale is likely to be to the student, for whom it is much less suited. The actions of the substances dealt with are almost always well described, and the information is reasonably up to date. But this is not a book on which the student should rely, because no space is given to mechanism of action, with which a work on pharmacology should be primarily concerned. For example, it is not enough to say that "ephedrine delays the destruction of adrenaline in the tissues and so prolongs its action." As an explanation of the mechanism of ephedrine action this is wholly inadequate.

There are a number of points where the best information is not given. Thus it is stated, as was formerly believed, that sulphaguanidine is only slightly absorbed from the alimentary tract. It is now known that, though it is absorbed slowly, much sulphaguanidine is absorbed; unlike sulphasuxidine, which remains in the intestine. Acriflavine is said not to affect phagocytosis; this again is erroneous, for antiseptic concentrations kill polymorphonuclear leucocytes.

A SURGEON'S PHILOSOPHY

Meaning and Purpose. By Kenneth Walker. (Pp. 170. 7s. 6d.) London: Jonathan Cape.

This book represents another rung on the ladder by which Mr. Kenneth Walker is climbing, from the contemplation of the genito-urinary system of the human being to a philosophy of the universe; and a very interesting rung it is. It is written with all the clearness and lucidity of style we have come to expect from Mr. Walker. In this book he reviews the various doctrines which he has accepted with greater or less enthusiasm during his life and for the most part found wanting. If he has not yet reached a completely satisfying philosophy to put in their place, how shall we blame him?

He points out that, in spite of close observation, scientific knowledge is necessarily indirect and that Western civilization has not made a sufficient attempt to improve the faculties of reasoning and reflection. Science firmly rejected metaphysics when it began to make real advances, but now we find that physicists have been compelled to become philosophers. After all, Plotinus said that intuition transcends experiment and reason, and this was accepted till the nineteenth century, when the real fight between science and religion began with the efforts of science to explain everything in terms of materialism, then of vitalism, then of mechanism. But all these approaches were one-sided because they forgot or ignored mind and epistemology (knowledge). With Darwin the scientists thought they had won battles, and the *Origin of Species* became for a time as authoritative and uncriticized as was the Bible for the diehard religions. With the growth of exact genetics, and the discovery of mutations the majority of which did not persist, Darwinism became difficult to accept; in fact it could not be accepted unless some form of central purpose in the evolution of the universe was admitted. The next step was the rise of the various psychologies based on (*a*) biology—the observation of animal behaviour; (*b*) physiology—the conditioned reflex of Pavlov and the behaviourism of Watson; and (*c*) medicine—Freud and those who followed him. All these are incomplete though all contain "truth." In spite of what the scientists have said, meaning, purpose, and intelligence do exist, and these are concerned with the "why" of evolution; whereas science is concerned with the "how." Attempts to answer this "why" were made by Bergson with his *élan vital* and by Ouspenski with his "Great Laboratory." Man is conscious of a purpose, and this is the province of religion which he cannot do without. Faith is essential to man, and the solution may be through the mystics and the affective realization that God is Love.

Mr. Kenneth Walker then goes on to discuss the three religions of modern times. First, humanism—the worship of man with the corollary of the emergence of a superman. This may be hastened by the second religion, the worship of race—the herrenvolk. But the psychology of the crowd is always at a lower level than that of the individual and is bound to produce war. The causes of war are economic circumstances, man's social state, and his acquisition of wealth. The third religion is that of communism—aiming at an aristocracy of power rather than of wealth, which may also lead to war. The promise of the future does not lie in these or in science, which alone cannot achieve truth; yet modern physics makes possible a liaison between science and philosophy; and an integration of philosophy into something higher than has yet been reached is necessary to avoid war and lay the foundations of a brighter world order.

MEDICAL LEXICOGRAPHY

The American Illustrated Medical Dictionary. By W. A. Newman Dorland, M.D., F.A.C.S. Twentieth edition. Revised and enlarged. (Pp. 1,668, with 885 illustrations, including 240 portraits. Plain edition 42s.; thumb-indexed 45s.) Philadelphia and London: W. B. Saunders Company. 1944.

The ever-useful *Dorland's Medical Dictionary* appears in its twentieth edition, thoroughly revised and brought up to date. All departments of medicine and surgery have been covered, and hundreds of fresh terms used in the fields of biochemistry, chemotherapy, allergy, specific therapy, endocrinology, vitamin research, tropical and parasitic diseases, and mycology have been incorporated, together with the names of a host of new synthetic and medical preparations. The vocabulary of war medicine and surgery, too, has received special attention. It is to be noted that the terminology employed is that of the *Standard Nomenclature of Diseases and Operations*, published by the American Medical Association, and edited by Dr. Edwin O. Jordan.

A close study of Dorland's dictionary seems to indicate that there are broadly two kinds of definition: one supplied by experts in the particular branch of medicine represented by

the word defined, and the other supplied by men with lexicographical talent but no expert medical knowledge. For example, the word "enteric" is defined as "pertaining to the intestines," but no reference is made in this entry to the common use of this word in "enteric fever": "enteric fever" does appear under the general entry "fever," as a synonym for typhoid fever, but not in the entry for "typhoid fever." Some definitions are tantalizing because they are incomplete. "Vitapathy," for example, is defined as "a modern system of quack medicine," but the definition does not tell us what the system is; as it is probably of limited interest, it seems unnecessary to give a separate entry: "vitapathic," with the definition "pertaining to vitapathy." In these days medical terms spring up like mushrooms in the night, and one of the great merits of Dorland's dictionary is the speed with which new words are incorporated in successive editions. At the same time we feel that this excellent work could be made still more serviceable if some of the dead wood were cut away, and if words not strictly medical were omitted. There would seem, for example, to be no point in including the word "voluptuous," well defined in any English-language dictionary, and still less reason for including the delightful but unusual word "volupty," the meaning of which is defined as "sensual enjoyment"—less bashfully defined in Webster's dictionary as "sexual enjoyment." Among the relatively new terms we note the word "geriatrics"—"that department of medicine which treats of the clinical problems of senescence and senility, geriatric medicine." There is, incidentally, no separate entry for the word "geriatric," but there is one for "geratic." Pursuing other cognate words, we note "geratology" and "gereology," both of which mean "the science whch deals with old age and its phenomena." Then there is the word "gerontology"—"the scientific study of the ageing process, its phenomena, diseases, etc." The compilers of the dictionary are to some extent bound to follow the current usage of words among medical writers. But that editorial pruning hook—the blue pencil—might perhaps have been used more ruthlessly; and, too, the word "geratology" was some time ago given a definition which would seem worth preserving. The *Shorter Oxford* defines it as "the science of the phenomena of decadence, esp. in a species of animals approaching extinction." Those who share the reviewer's taste for dipping into dictionaries will find they get as much pleasure out of a medical dictionary as out of any other, and may even share his delight at discovering the word "gephyrophobia," which means "fear of walking on a bridge, river bank, or other structure near the water."

Notes on Books

Prof. ARNOLD SORSBY's thoughtful and stimulating book *Medicine and Mankind* was reviewed in these columns on Dec. 13, 1941. An abridgment from the fuller work has now been published by Watts and Co. as No. 104 of their series, the Thinker's Library, at 2s. 6d. This will ensure a wider public for the author's account of the meaning and mechanism of health and disease, and of the conceptions and aims of medicine.

The pamphlet by Lord HORDER (in collaboration with the Empire Rheumatism Council) entitled "Rheumatism. Notes on its Causes, its Incidence, and its Prevention; with a Plan for National Action" was first published in March, 1941. A fourth edition, the text practically unchanged but with a new preface, makes the total printing 7,000 copies. It is published by H. K. Lewis and Co. at 2s.

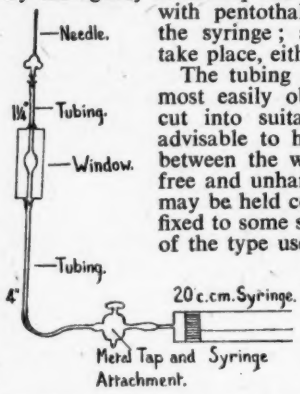
Three pamphlets by Dr. EDWARD F. GRIFFITH (H. K. Lewis and Co.; 1s. 6d. each) are the lectures which form the second part of his book *The Road to Maturity*, reviewed in these columns on June 3 (p. 754). They are useful guides in sex education, though it is not desirable that lectures on such subjects should be stereotyped, since their form and substance must vary with both the audience and the lecturer. *Facts in Development* is a biological account of reproductive function from the amoeba to man. *Emotional Development* deals with the mental side of sex and touches on masturbation, homosexuality, and the guilt feelings which are liable to arise from them and the emotional differences between the sexes. *Towards Maturity* deals with the problems of preparation for marriage, family limitation, premarital relationship, prostitution, and other related questions.

Preparations and Appliances

CONTINUOUS PENTOTHAL ADMINISTRATION

Dr. W. G. MCKINNEY (Londonderry) writes:

I have found the actual giving of continuous pentothal solution simplicity itself by means of the apparatus illustrated. There is nothing very original about it except the little tap mount, in which the 20-c.cm. syringe securely fits. The introduction of the tap into the apparatus is obvious, as allowing the syringe to be detached for refilling during the course of a prolonged operation, especially if 2½% solution is being used. By the agency of the tap the whole system can be left charged with pentothal solution during detachment of the syringe; and clotting definitely does not take place, either in the needle or in the tubing.



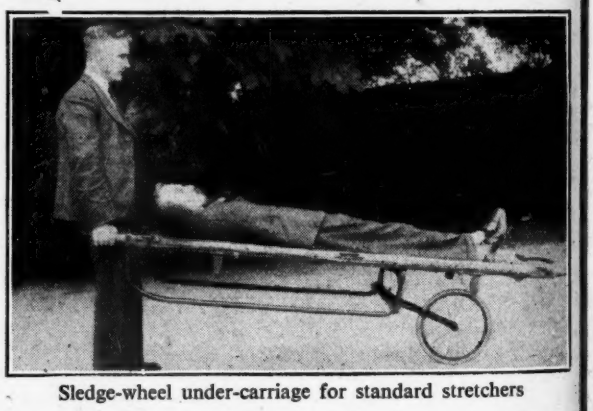
The tubing used is of very fine bore, and is most easily obtainable as an infant's catheter cut into suitable lengths or portions. It is advisable to have some four inches of tubing between the window and the tap to allow for free and unhampered use of the syringe, which may be held comfortably in hand or, if desired, fixed to some simple rack fitting. The window is of the type used frequently as a syringe attachment for the injection of varicose veins, and serves admirably as a visual guide to the true intravenous position of the needle.

Of the needles which I have used, size 12 intravenous, made by Allen and Hanburys, is without doubt the best and most satisfactory. When properly in position it is securely fixed to the arm by means of a piece of narrow strapping passing over the mount. Another piece of strapping at the lower end of the window gives extra stability and freedom from worry about drag on the needle-point. The syringe may be either eccentric or concentric nozzled: it makes no difference. The patient's arm is supported on an arm-rest and firmly fixed thereto by means of a wrist-strap or bandage.

Using this simple and readily procurable apparatus I have given pentothal continuously on numerous occasions and have had no trouble with needle blockage, leakage, or air bubble.

UNDER-CARRIAGE FOR SLEDGE STRETCHER TRANSPORT

Lieut.-Col. D. G. DUFF, F.R.C.S.Ed., writes: The advantage to be got from sledge stretcher transport in minimizing shock to the patient and hard labour to the bearers are undeniable. A practical test against any other stretcher assembly (especially in hill country) will quickly convince anyone. The incorporation of sledge runners, especially in a tubular metal stretcher, need not add much to the weight. It adds greatly to the utility, while preserving all the traditional usages (*Lancet*, June 17, 1944). Since, however, there may be reluctance to scrap existing stretchers, an under-carriage has been designed and made to fit the standard wooden stretcher. It weighs about 9 lb., but will save many foot-pounds of energy expenditure. With a central wheel applied it will take practically all the strain off stretcher-bearers. On occasion it will allow the wheelbarrow *modus operandi*, so that one bearer can carry his patient with less exertion than is required from either of the normal two bearers. The accompanying photograph shows the wheelbarrow position. The central position with vertical wheel forks is better, as it takes all the weight from the two bearers



Sledge-wheel under-carriage for standard stretchers

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SATURDAY DECEMBER 9 1944

THE GERMINAL EPITHELIUM AND THE PROSTATE

A hormone secreted by the germinal tissue of the testicles has often been postulated but never hitherto proved. The question is one of more than academic importance, for one hypothesis (advanced by Lower) to explain senile prostatic enlargement involved the assumption of such an internal secretion. Lower and his colleagues assumed that with advancing years this secretion decreased, and that the anterior pituitary was thus induced to increase its output of gonadotrophin, just as in the menopausal woman the output of gonadotrophin is increased by ovarian failure. The gonadotrophin, acting on the still functional interstitial cells of the testicles, gave rise in their hypothesis to an increased output of testosterone, which caused enlargement of the prostate. Unfortunately for this neat hypothesis, it is impossible to produce by the administration of testosterone a condition resembling benign enlargement as it occurs in man. The prostate hypertrophies but remains histologically normal. A second hypothesis is diametrically opposed to that of Lower. It takes no account of an internal secretion of the germinal epithelium, and is based on the fact that the normal man secretes both androgenic and oestrogenic hormones, the former from testicles and adrenals and the latter from some tissue or tissues hitherto unknown. That the oestrogen-producing tissue also is within the testicle is made probable by the observations that animal testicles contain an oestrogen and that the testicles and urine of stallions are very rich sources of oestrogens. It assumes that with advancing years the secretion of testosterone diminishes with no corresponding decrease in oestrogen and that the unopposed oestrogen is responsible for the prostatic enlargement. That oestrogen does in fact cause prostatic enlargement was independently shown by Lacassagne, by de Jongh, and by Burrows and Kennaway. The hypothesis was given still further experimental support by the work of Zuckerman and his colleagues, who showed that the changes induced were due largely to the sensitivity of the prostatic utricle and its bed (the "middle lobe" of the surgeon) to oestrogenic stimulation; that in the dog there occurs spontaneous prostatic enlargement indistinguishable from that induced by oestrogens; and that the effects of oestrogens can be prevented by the simultaneous administration of androgens, especially testosterone propionate. The changes induced in animal prostates by oestrogens bear some resemblance to benign enlargement in men, and the dissimilarity may possibly be explained by species differences in the embryology of the uterus masculinus. Treatment based on this hypothesis has unfortunately not proved wholly satisfactory, and such "successes" as have been reported have been uncontrolled.

Whether or not either hypothesis represents part of the truth, it is obviously of the greatest importance to elucidate further the endocrine function of the testicles. Törnblom[1] has described a series of beautifully planned experiments with this in view. He showed that giving testosterone to young castrate rats in such quantity that the weight of the prostate and seminal vesicles exceeded somewhat the weight of these organs in whole animals did not prevent the increase in weight of the pituitary which occurs after castration. It follows that some other hormone must be normally formed in the testicles the effect of which on the pituitary is greater than its effect on the prostate and seminal vesicles. By treating the testicles of rats with *x* rays it is possible to cause atrophy of the germinal tissue without affecting the interstitial cells. In such animals the weights of the prostate and seminal vesicles are unaffected, but the weight of the pituitary is increased. It follows from this that the hormone the absence of which causes the increase in weight of the pituitary is formed in the germinal epithelium. Moreover, when the difference in radiosensitivity of the two testicular tissues was increased by stopping the testicular circulation during treatment, a weight increase occurred in both the pituitary and the accessory sex organs. This may possibly be explained on the supposition that the inhibition of secretion in the germinal epithelium causes overactivity of the pituitary and thus of the interstitial cells, with the resulting enhanced androgenic effect upon the prostate and seminal vesicles. In his next series of experiments Törnblom succeeded in isolating a fraction from testicular tissue which prevented the increase in weight of the pituitary in castrate rats without influencing the weight of the accessory sex organs. It therefore possessed the postulated properties of the germinal-tissue hormone. When isolated it was found to possess all the biological properties of oestradiol, and all its actions could be exactly reproduced by oestradiol. No evidence of any non-oestrogenic substance having the postulated properties of germinal-tissue hormone could be found.

An attempt was next made to show directly an increase in gonadotrophic hormone by a new experimental method. An increased formation of gonadotrophin causes the ripening of follicles in infantile ovaries implanted into the kidneys and a secondary oestrous reaction in pieces of vagina implanted in muscle. By this method the enhanced production of gonadotrophin after castration can be demonstrated. Unfortunately no such increase could be demonstrated after inhibition of the germinal-tissue secretion only. This is the only gap in the experimental proof of Törnblom's thesis, but it is not a very serious one, for, as he points out, the production of pituitary gonadotrophin is inhibited by both testicular hormones, and it is naturally not so stimulated by the absence of one as by the absence of both.

It is only in his last chapter that Törnblom leaves the straight path of close reasoning which he has clearly set himself. Having established that the cessation of the

[1] *Uppsala LäkFören.*, 1942, Häft 1, och 2, p. 1.

internal secretion of the germinal tissue causes an increased secretion by the interstitial tissue, he asks the question: "Is hypertrophy of the human prostate due to a corresponding functional disturbance?" To answer this question he treated dogs with testosterone propionate, choosing dogs because they are the only animals known to suffer from spontaneous prostatic enlargement. He confirmed the work of previous investigators who have shown that it is possible by such means to cause prostatic enlargement and even urinary obstruction. Histologically the enlargement was found to be due to a diffuse homogeneous hyperplasia. It resembled one type of spontaneous enlargement seen in dogs, but it did not resemble human benign enlargement. Zuckerman and Groome have already pointed out that in most instances the spontaneous prostatic enlargement of dogs is not histologically abnormal and have suggested that it may well be due to excess of male hormone. They described, however, a case in which the enlargement was histologically abnormal and similar to that which can be experimentally induced by oestrogens. They point out, also, that, on the assumption that the common type is due to excess of testicular androgen and the less common type to excess of testicular oestrogen, Hobday's successful treatment by castration is readily understandable in both conditions. Without committing himself to a definite statement, Törnblom appears to suggest that his proof that the germinal epithelium of the testicles of rats elaborates oestradiol supports the hypothesis of Lower that human prostatic enlargement is due to excessive androgenic stimulation. It may equally well be taken as supporting the contrary proposition. It is clear that no final decision can be reached until more is known about the effects on the human prostate of administered androgens and oestrogens.

EGGS AND SALMONELLA INFECTIONS

Knowledge of the reservoirs of *Salmonella* infections in different animals is steadily growing, and explains both their wide distribution as a cause of animal diseases and the various ways in which the causative bacteria can obtain access to man. Ducks' eggs were known as a source of *Salmonella* food-poisoning as far back as 1926, but their significance was not realized in this country until the publication of an important paper by the late Dr. W. M. Scott[1] in this *Journal* in 1930. Since that date more facts have come to light. It is now known that ducks may suffer from epidemics of *Salmonella* infections, and that, while the bacilli may be extraneous organisms passing from contaminated material through the porous egg-shell, others are present in the egg yolk and are derived from specific infections of the ducks themselves. Certain varieties of ducks seem to be especially liable. While outbreaks are commonest in some Continental countries, particularly Holland and Germany, they are not unknown in Great Britain. J. S. Garside and R. F. Gordon[2] described an extensive outbreak in 1938–9 in which *B. enteritidis* and *B. typhi murium* were recovered from 44 ducks whose blood contained *Salmonella* agglutinins; but *Salmonella* strains were not recovered from the eggs of the infected birds. This was not the experience in other outbreaks, and several strains have been isolated; by far the most prevalent are *B. enteritidis* (variety Essen) and *B. typhi murium*. In Holland the duck industry is an important one, and in 1940 C. F. Van Oigen[3] described the extensive investigations undertaken by the Netherlands Egg Control Bureau to stop the spread of *Salmonella* infections. Their report shows that there is no one ready remedy which is satisfactory, but that by blood agglutinin tests, segregation, and examination of eggs the number of infected eggs can be reduced to small proportions. The use of pasteurized frozen eggs is quite satisfactory.

The egg of the hen has a much cleaner record. There have been at the most only one or two food-poisoning outbreaks which might be ascribed to the use of infected eggs (excluding dried eggs). While infections with *Salmonella* strains in hens have been fairly numerous—and expensive to breeder and owner—almost always the source of infection has been *S. pullorum* or *S. gallinarum*, strains not pathogenic to man. Recent work shows, however, that more toxic strains may be present. For example, W. L. Mallmann, J. F. Ryff, and E. Matthews[4] isolated a variety of *Salmonella* strains from diseased hens sent to them from various parts of Michigan, U.S.A., including such types as *S. oranienburg* known to have caused human food-poisoning. None of them, however, produced any symptoms when fed in large doses to monkeys. With a true bill against the duck and something of a "non-proven" verdict against the hen, the question of infection from dried eggs and egg powders has to be considered. N. E. Gibbons and R. L. Moore[5] have recently given some important information on the subject. They examined for *Salmonella* types 380 lots of Canadian egg powder produced from November, 1942, to December, 1943. Organisms were found in 28 samples (7.4%): 9 different types were isolated—*S. bareilly* (11 lots), *S. pullorum* (5), *S. oranienburg* (4), *S. typhi murium* (3), *S. thompson* (2), *S. minnesota* (2), *S. newport* (1), *S. potsdam* (1), and *S. manhattan* (1). Except *S. pullorum* all strains are potentially pathogenic to man. In the samples for which numerical estimations were made the actual number of *Salmonella* organisms present was low, mostly less than 1–10 per gramme, but one sample contained 54 per gramme. Their presence was not related to general contamination as judged by coliform estimations. No information was available as to how these *Salmonella* strains gained access to the egg powder. In a second paper[6] the authors investigated the effect of drying, storage, and cooking on the *Salmonella* content. They found that over 99% of the organisms in heavily inoculated liquid egg were killed on drying in an experimental spray drier, and concluded that similar results would be obtained in commercial driers. Storage also is inimical to their survival, and they rapidly diminish in number, surviving the longer the lower the temperature. In cooking experiments with reconstituted eggs heavily inoculated with Salmonella organisms they found that the bacilli were all destroyed in egg powder cooked as scrambled eggs and omelettes, and in sponge cakes, custards, and muffins. They therefore consider it is debatable whether the contamination of egg powder with *Salmonella* organisms can be regarded as a health hazard. But F. Sieke[7] found that

[1] *British Medical Journal*, 1930, **2**, 56.
[2] *J. comp. Path.*, 1940, **53**, 80.
[3] *Tijdschr. v. Diergeneesk.*, 1940, **67**, 280. Summary in *Bull. Hyg.*, Lond., 1940, **15**, 437.
[4] *J. infect. Dis.*, 1942, **70**, 253.
[5] *Canad. J. Res.*, 1944, **22**, 48.
[6] Ibid., p. 58.
[7] *Arch. Hyg. Bakt.*, 1943, **129**, 108.

boiling ducks' eggs in the shell for shorter than 8 minutes would not make an infected egg harmless.

The present position would seem to be that we cannot entirely exonerate dried eggs from the possibility of acting as a vehicle for the spread of *Salmonella* poisoning, although the risk is probably small. Actually outbreaks in this country of *Salmonella* food-poisoning associated with dried eggs are not unknown during the present war, although none has apparently been the subject of a scientific paper.

THIOCYANATES AND THIOURACIL

Sodium and potassium thiocyanate have been used for the treatment of hypertension since Pauli in 1903 discovered their property of lowering blood pressure. While many doubt their efficacy, others are certain that some patients derive benefit. The mode of action of thiocyanates does not appear to have been defined, but the recent evidence concerning substances like thiouracil which affect the thyroid gland probably throws some light upon it. Astwood[1] has shown that when thiouracil is given to rats an enlargement of the thyroid gland follows. From the work of the Mackenzies[2] and of Astwood and his colleagues[3] it is known that this effect occurs only when the pituitary gland is present, and that it is accompanied by a fall in the basal metabolic rate. Thiouracil, it is concluded, depresses formation of the thyroid hormone in the thyroid gland, and, because of the consequent fall of thyroxine in the blood, the anterior pituitary stimulates the thyroid gland so that this becomes hyperplastic. Thiouracil is now used in thyrotoxicosis because it diminishes the formation of thyroxine, and therefore causes the B.M.R. to fall.

Among the substances which Astwood found to cause hyperplasia of the thyroid gland of rats was potassium thiocyanate. It is evident, then, that if patients receive potassium thiocyanate for long periods of time for the relief of hypertension the same symptoms will probably appear in them as have been observed in rats. Foulger and Rose[4] describe precisely this occurrence in one patient, and Rawson, Hertz, and Means[5] describe it in two others, citing more from the literature. In Foulger and Rose's case—that of a woman treated with 0.3 g. potassium thiocyanate daily from March, 1938, to July, 1939—the blood pressure fell from 210/110 mm. to 175/110 mm. In September, 1940, when she was still receiving thiocyanate, she had diffuse enlargement of the thyroid, the B.M.R. was −11%, and there were general symptoms of hypothyroidism; she was therefore given thyroid together with the thiocyanate, with the result that the symptoms cleared up. Later the thyroid was stopped and the symptoms then reappeared. It was finally recognized that the thiocyanate was responsible for the hypothyroidism, and when thiocyanate was stopped the puffiness of the face, the swelling of the gland, and the low B.M.R. disappeared. It is clear from this and other cases that so far as their effect on the thyroid gland is concerned thiocyanates, thiourea, and thiouracil are identical.

The question remains why thiocyanates benefit hypertension. Is it because of this action on the thyroid gland? Does the blood pressure fall because the B.M.R. falls? Rawson, Hertz, and Means[5] apparently do not think so; at least they state that "thiocyanate goitre can be relieved by the administration of thyroid even when thiocyanate administration for hypertension is continued." Perhaps they have not considered the point in the form in which it is now presented. It is to be remembered, however, that Blumgart, Levine, and Berlin introduced total thyroidectomy as a treatment for angina pectoris, a condition not unconnected with hypertension. If thyroidectomy benefits patients with angina pectoris, and if thiocyanates, which diminish thyroid function, benefit patients with hypertension, there is some likelihood that thiocyanates act in hypertension by diminishing thyroid function. If so, thiouracil should also be of value in hypertension, and might suitably be tried. Astwood, to whom we owe the introduction of thiouracil for thyrotoxicosis, chose it in preference to thiocyanates and other substances because of its lower toxicity.

[1] *J. Pharmacol. exp. Therap.*, 1943, **78**, 79.
[2] *Endocrinol.*, 1943, **32**, 185.
[3] Ibid., 1943, **32**, 210.
[4] *J Amer. med. Ass.*, 1943, **122**, 1072.
[5] *Ann. intern. Med.*, 1943, **19**, 829.

SUPPLY OF MEDICAL BOOKS

As fellow-sufferers under the rationing of paper and the shortage of skilled labour we sympathize with medical publishers in their wartime plight. A memorandum on the inadequacy of the supply of medical books in relation to present and future needs has been drawn up by the Medical Group of the Publishers Association (28, Little Russell Street, W.C.1). This explains the present serious situation with regard to the supply of books on medicine and its basic sciences, nursing, pharmaceutics, veterinary science, etc. It urges that adequate measures should be taken to remedy the acuteness of the long-existing shortage of such books. No improvement can occur until the Government makes more paper and labour in the printing and binding trades available for educational books. Medical publishers are responsible for maintaining the supply of textbooks, works of reference, and monographs for doctors, research and laboratory workers, medical and dental students, nurses, pharmacists, veterinarians, and all classes of medical auxiliaries. The growth in the numbers of students and practitioners has greatly increased the demands of the medical profession; and the same is true of nurses, pupil midwives, and students of first aid. Meanwhile the requirements of the oversea market are at least twice as great as in pre-war years, for the Empire very largely depends for its supplies on publishers in Great Britain. Various economies have been, and are being, achieved in book production by medical publishers, but these cannot effect a substantial saving. Some medical books are out of print solely because the paper for them is lacking; this applies to textbooks of major importance, and particularly to nursing textbooks. The need for providing reprints and revised editions on the limited paper quota has diminished the production of new medical works, more particularly books on war medicine and surgery wanted urgently for the higher professional education of medical officers in the Forces and the E.M.S. Having already made the point that a distinction should be drawn between "medical books" as understood by us and popular books on medical matters for the general public, the memorandum shows how the shortage of medical books is due to a diversity of causes. Early release of key men to the printing, engraving, and binding trades would have a profound influence if coupled with a less meagre supply of paper. We are at one with the Medical Group of the Publishers Association in urging that the special problems connected with the production of medical books and journals demand full and early consideration. Medicine cannot advance without books and reputable periodicals. Even if the existing difficulties were remedied to-day the demand would long continue to outrun productive capacity. There is bound to be an increasing call both for books that have gone out of print during the war and for new books designed to meet the needs of the

changing curricula of the medical and nursing professions; moreover, the activities of the British Council are stimulating the market for British medical books abroad.

LOGIC AND MEDICAL RESEARCH

Of some men it can be said that whatever they write is valuable, whether the conclusions reached are right or wrong. Nobody doubts now that *The Conduct of the Allies* was bitterly partisan and that *Reflections on the Revolution in France* was coloured by prejudice and violent emotion; but nobody could read either without pleasure and intellectual profit, because Swift's power of lucid and telling argument commands admiration and Burke cannot write a page without some flash of beauty or of insight into human nature. The writings of a third great Irishman, Sir Almroth Wright, have the same effect. Like Swift and Burke, he has been engaged in many controversies and, like them, he has not always been just to points of view with which he has no sympathy; but whatever he has written bears the hall mark of genius. His reprinted paper on Induction[1] contains some passages which a reader familiar with the statistical methods despised by laboratory workers, and indeed in their early childhood a generation ago, but now almost universally adopted, must think inexact; but even statisticians can learn something of value from the censures. There is a danger—not threatening statisticians alone—that some men will believe that Nature's secrets can be wrested from her by anybody who has learned a sufficiently elaborate technique. "Pray, what do you mix your colours with, Mr. Opie?" "With brains, Mam." Brains are as important in the art of medical research as in that of painting; in both technique is important too, but secondary. The Wrights, like the Opies, are contemptuous of mass-produced research. Blackmore, better known as a versifier than as a physician, was a pupil of Sydenham, and when he asked his master what he should read was told to read *Don Quixote*. Dr. Johnson reproved Sydenham for jesting, but perhaps the great man intended to convey to his pupil the truth that it is not by reading books one becomes a physician. One cannot learn from books how to become a great researcher. Something can be learned by study of masterpieces, although even then there is the difficulty familiar to students of the noble game of chess. One need not be an adept to be thrilled by the way in which a Morphy or a Lasker destroys his antagonist in a few moves, by, shall we say, a crucial experiment. But the student—unless himself a Morphy—only learns a little, a very little, of the process which enabled Morphy to make the crucial experiment, and will not learn it from treatises on "openings." That is one of Sir Almroth's lessons: the amount of pains, imagination, and hard thought which prepare the way to a crucial or decisive experiment. It is possible to help a beginner by a logical analysis of methods of discovery. Here again the humble analogy of a mere game is serviceable. A famous teacher of chess of the last generation, James Mason, once said that a careful study of a few of the stock methods of beginning a game was of much more value than trying to learn the tricks of this or that gambit. Sir Almroth helps the student by contrasting the various senses or connotations of the term "induction" and the shades of meaning of "control" as used in clinical or laboratory research. He proposes a new terminology which seems to us good, although the modern prejudice against "dead" languages may hinder its adoption. He makes good play with the dangers of under- or over-simplification in experiment; in his terminology, hypoclaustration and hyperclaustration. The former he illustrates by the conclusion of the Victorian physiologists that nutrition was explicable on quite simple physical analogies; the experimenters had not realized adequately that there was a difference between supplying calories and giving foodstuffs. The latter he illustrates by the remark that to test the value of antiseptics by successive dilution with water fallaciously omitted albuminous substances which operate as quenching and buffering advects whenever antiseptics are employed in local treatment or are administered internally.

Few readers will agree with all Sir Almroth's conclusions; still fewer will not profit by a careful study of the essay on Induction. The word "research" has propagandist value now; it is good that young people should learn that it is not much easier to enter the kingdom of genuine research than the kingdom of heaven.

1 *Studies on Immunisation.* Second Series, Vol. IV, Appendix IV, "On Induction in General," Heinemann, 1944.

WAR AND MENTAL HEALTH

For reasons of paper economy the annual reports of the Board of Control are not being printed or put on public sale during the war. Its example might well have been followed more widely. Summing up the effect of war on mental health, the Board finds no evidence that the war has brought about any increase in serious cases of mental breakdown. Though admissions to mental hospitals do not by themselves give a complete picture of the incidence of psychosis and neuropsychosis, they indicate the general trend. Even in the "blitz" areas there are relatively few cases in which the mental breakdown can be attributed with certainty to the effects of war and more particularly of air raids. Where breakdown appears to have been caused or accelerated by air raids it is generally found that the patients' past history suggests that they might have developed mental trouble in any event, though possibly at a later date. A recent neurosis survey carried out by the Ministry of Health did not show any alarming increase in neurosis, particularly when allowance was made for the fact that the war had forced into industry, often in unfamiliar and trying conditions, many who previously led sheltered lives and whose breakdown under unaccustomed strain might have been thought inevitable. "Looking at the situation as a whole, we feel that it may fairly be claimed that the war has demonstrated the mental stability of the nation." The Board, at the request of the War Office, has organized a scheme of after-care for Service patients discharged from special hospitals and E.M.S. centres on account of psychiatric disability or mental abnormality. The aim is to secure that patients will, on discharge, know where to look for skilled treatment and advice. In co-operation with the Ministry of Health the Board has also undertaken a follow-up of ex-Service cases of this kind. Such inquiries will be purely fact-finding and will not overlap the after-care scheme; they will cover cases discharged from the Army through E.M.S. neurosis centres. The Board is also assisting the War Office in a follow-up of cases discharged from military mental units; wartime difficulties of staff, however, will not permit detailed inquiries now, but when the investigation can be completed "it should throw valuable light on the success of modern methods of treatment." At the end of 1943—the year covered by the Board's 30th report—the number of persons suffering from mental disorder notified as under care in England and Wales was 147,557 (63,054 men and 84,503 women), and over 86% of them were being treated in mental hospitals provided by local authorities.

PREAMBLE TO POST-WAR FOOD EDUCATION

BY

F. LE GROS CLARK, M.A.

We have made during the war a far more systematic attempt than ever before to influence the public in the choice and preparation of their food. The scope and plan of the wartime campaign will be briefly examined below. The question that naturally arises at the present stage in our affairs is this: What are our prospects of continuing this wholesome work in more normal times, and what are the conditions for its success?

But, first, how far will this leaven of teaching and persuasion be necessary after the war? We can argue for it in this wise. A sound dietary is part of the broad basis of social stamina and good health; and we may assume that a fair proportion of our annual expenditure on ill-health is indirectly attributable to poor feeding. The exact proportion could scarcely be demonstrated; but the evidence is sufficiently good to make it worth our while to see whether we can effect a saving. This, however, is still a matter of persuading the public to eat the right food, even where wage-levels and prices are so adjusted as to allow a reasonable standard of consumption; the food may be available, but it does not follow that it will be consumed. The truth is that when a civilized community has a very wide choice of foods there is nothing in Nature to prevent it from adopting the most lamentable pattern of food habits; and within that pattern of food habits it will live and die for all time unless some effort is made to change the pattern. It is useless to hope that tastes and habits of this kind possess some internal power of effecting their own improvement. Man is an omnivorous animal, a fact to which, no doubt, he in some measure owes his survival; but he is ill supplied with instincts in the choice of food; and he has to pay for his survival by gradually shifting the choice of his foods on to a rational level. He will otherwise, since he is obviously not protected by instinct, be subject merely to a mass of whims, traditions, customs, and cravings.

In that case the work might as well be undertaken. There is no chance that a brief campaign will have any effect whatsoever; this is a job for a lifetime. It is one, moreover, that needs strict scientific method and an appreciation of the anthropological material with which we are dealing. The technique is that of the leaven and not that of the textbook. Provided we understand this and admit the premisses, there seems good reason for continuing our campaign of food education, even if we have to adapt our style and our methods to the conditions of peace.

Food Advice Centre

The structure assumed by the present campaign is somewhat after this manner. Most of the work is fostered by the Ministry of Food, in the sense that considerable funds are required and that the Ministry is naturally felt by a people at war to be the well-head of sound advice in the matter of food. The other Departments and the voluntary organizations, that all have their part in the work, acquire a peculiar virtue in the mind of the public through their association with the Ministry. The Ministry of Food may properly deny that it is more than an equal partner in this campaign with the Ministries of Education and Health; but the fact is that "food" to the public means the Ministry of Food.

The immediate contact the Ministry has with the public lies, of course, through the Press, the radio, the leaflet, and the poster. Its more pervasive influence is exerted through two special devices—that of the "food advice centres" and that of the "food leaders' schemes." These are perhaps the most interesting aspects of the whole campaign. All else that the Ministry has done by providing itself with experimental and practical kitchens and developing an effective news-letter and bulletin service is merely what any serious organization of the kind would do if it had the funds.

The method of the food advice centre is that of renting a shop in a good thoroughfare, equipping it for cookery demonstrations, and staffing it with two or three qualified women. Centres of this nature were first opened by the Ministry in 1940, and there are now some 40 of them. It is, of course, obvious that the direct influence they can have reaches a very small percentage of the public. As often in cases of this kind, a centre or a shop window may vaguely affect the public mind by its mere existence; it impresses upon the shopping women of an area that food and cooking are matters of national interest, even if no more than 10% of them enter the premises or pause to study the window display. But it would be almost impossible to assess the extent of this influence. As time went on, the centre became rather the office of the organizer, from which she might arrange for the delivering of lectures or demonstrations in factories, village halls, and so forth. The ability of two or three qualified women to permeate a large area was really the factor that counted; and the technique of the travelling van, of the news-letter, of the shop display, and of the poster have all been tried.

Food Leaders' Scheme

But by 1942 it was evident that a very large proportion of housewives were still uninfluenced to any calculable extent. Some new device was needed for the dissemination of elementary teaching. The earliest of the food leaders' schemes was initiated in Birmingham, and they have since spread rather unevenly through the West Midlands and the Home Counties, with a gradual but perceptible growth elsewhere. It must be noted that here the Ministry of Food assumes no direct responsibility, though in practice a fair amount of the basic work has usually to be undertaken by the food advice organizers. The idea of street or village "food leaders," who would transmit advice and information to their neighbours, was soon realized to be insufficient unless it were associated with some kind of elementary classes for the prospective leaders. This not only brought the schemes within the sphere of what is known as "adult education" but it might imply that premises would at times be needed for the holding of classes. Now, it is the Ministry of Education that is responsible for adult education; and, so far as the Ministry of Food is concerned, almost the only available premises in any area are the schools. In practice, however, what has often happened is that the women's organizations, prompted by the Ministry of Food, have gone ahead with the selection of their prospective food leaders and, on making formal application to their local education authority, found it too short-staffed to undertake more than a fraction of the lectures that were needed. But the Ministry of Education remains ultimately the responsible department; and in theory the education authority of each area transmits to the local food advice organizer most of its functions in the training of the food leaders.

There was probably a further doubt that for a time affected the judgment of the Ministry of Food. The schemes had not been originated by the Ministry of Food, but by an education authority. The women they were intended to organize were almost entirely unqualified lay women, whose advice and counsel would presumably be sought and absorbed by an indeterminate mass of housewives. If there were in the recesses of the Ministry a few tolerant minds prepared to take the risk of something going wrong, several of the practising dietitians were more dubious. It was accepted, of course, that the food leaders were not to teach or lecture; they were to be no more than a leaven of right thinking in the urban streets and in the countryside. But the distinction could not readily be drawn; no one could forbid them to lay down the laws of correct feeding. In effect, the trained dietitians have not always been enthusiastic in their dealings with the local food leaders, even if they have done their duty by them: the two modes of teaching and persuasion have never quite fused into a single instrument.

Style of Wartime Food Education

But when we come to examine the literature of the movement, embodied in its pamphlets and news-letters, it occurs to us at once that, however enduring may be the knowledge imparted, the form and style of the teaching have almost invariably a wartime flavour. The reason given for the proffered advice is the scarcity of many foods; and the appeal is for housewives to play their part in maintaining the fitness

of a people at war. The assumption behind it all is that there will come a time when these motives will no longer operate. It is, in brief, a wartime movement only, and there can be no unbroken transition from the forms of war to those of peace. The fact is that the campaign is devised to catch the largest and least-organized section of our adult population, the housewives, and to draw it functionally into the total war economy. In its "food leader" aspect it meets a need, in that it attempts to resolve the self-contained lives of an increasing number of housewives into the common effort; it gives them the *raison d'être* for their many discomforts and supplies them with the first requisite of every trade or calling—a specialized and easily accessible literature. There is no question that the news-letters and pamphlets distributed from the local centres of instruction have a very unifying and stabilizing effect upon the communities they reach.

After the war we shall have a different and a somewhat more complex problem to face. Much of the way in which we re-orientate our campaign will depend upon the extent of the final rupture between war and peace. If all the forms and phrases of war lapse with the transition, the process of re-orientation will be far more tedious and debatable. Because of the prestige it has earned, and the common admission that if anyone has a right to talk about food it is a Ministry of Food, the survival of the Ministry even in a very modified form is a matter of some importance to us. It is an elementary fact that the teaching of other Ministries on the subject of food is suspect to many members of the public, and they would be well advised, perhaps, to leave most of it either to a reconstituted Ministry of Food or to some body contrived for the purpose, that will have to earn its reputation by its work.

No small part of the relative success of the Ministry of Food has been due to the fact that it has never announced any intention of *educating* the public; it has merely "advised" and "informed." We must recognize that the average adult woman in this country has no wish to be further *educated*, least of all in matters of diet; but she is quite prepared to assimilate learning about subjects that seem to her interesting or useful. If we want the post-war woman to absorb into her daily life the knowledge of food values we must make our matter both digestible and palatable. One lesson from our wartime experience seems clear; and that is that probably 90% of housewives will not come to formal classes and demonstrations. They may be led to do so in the future; for the moment they do not. The only obvious method of reaching them is through the technique of the social leaven, the stall in the market-place, the village expert, the informal parlour gossip, the flower-show quiz. We shall have to take our chance that from time to time some curious doctrine or twisted interpretation will gain credence; the risk has always to be taken by those who set themselves the slow task of changing the daily habits and the ingrained patterns of taste of a population. But we must recognize from the start the distinction made in the public mind between *health* teaching on such matters as venereal disease, diphtheria immunization, or dental treatment, and *food* teaching that has reference to a positive and daily satisfaction. The clinics, the medical practitioners, and the societies established for health propaganda can all play their part; but if the movement is to be effective it must mean by food precisely what the public means by food—that is, far more than a physiological basis for sound metabolism.

Changed Conditions of Peace

To what extent, then, may we assume that our wartime methods will have to be modified to meet the requirements of peace? Our main public is the community of housewives; and much will depend on our ability to maintain in the mind of the average housewife the sense of her social function. There is a risk that this sense will be lost when the close of hostilities relaxes the cohesive bonds that unite us in some measure towards a common task. It seems likely that the joint consultative committees of the women's organizations that have emerged in the course of the war will survive it and will provide a starting-point for the period of new construction. They account between them, it is true, for only a relatively small proportion of the housewives of the country; but they are a pervasive influence, and a joint committee of this nature can often take on a vitality of its own that transcends in influence the sum of its component parts.

What we have to seek is some method of creating a ferment of change in the views and practices of women in the kitchen. The concept of "food leaders" is the most satisfactory one that has so far emerged from our wartime experience. But there are two or three comments that must be made on the scheme as it might in theory be applied in a post-war economy. (1) We shall have, in my opinion, to discard the phrase "food leaders" and contrive a more suitable one. The term is accepted in war, when a nation takes on the semblance of an army; but it is only just accepted. There are even now some doubts whether the title and the badge may not arouse more resistance than respect among a woman's neighbours. (2) The flow of news-letters seems an essential feature of such a movement: it is both its pulse-beat and its organic unity. (3) The movement will have to be associated, both in the mind of the average housewife and in that of the dispersed body of women who have to do the work, with a source of authority that enjoys high prestige. What that source will be it is not for me to suggest: the practice in this country is often to establish a council with a certain degree of independence, which is known to possess the confidence of a State Department. (4) If there are a number of qualified women employed in the campaign, as at present, they will have to be selected not merely for their dietetic training but for their appreciation of the techniques that will be in use.

There are, no doubt, many among them who begin to comprehend their business as a branch of applied anthropology; but the merging of expert and inexpert functions should be more complete and durable than it has so far proved.

Basis of Post-war Food Education

There are two further aspects of a post-war campaign on which we may comment. It is a principle of educational theory that teaching in mature life is best associated with a practical job that concerns the learner; the confusion lies in our tendency to label this kind of teaching as merely *technical*, whereas it implies no more than that the job is the obvious point upon which we should concentrate. Now, a housewife's job is the buying, storage, and final preparation of the food; and the kitchen is her workshop. If the Ministry of Food survives the war in some form it might do worse than present itself to the public as essentially the housewives' Ministry; and the basic substance of our story should be the shopping basket and the kitchen stove. But we must by all means avoid concentrating our teaching either at the extreme of the "food values" kind of discourse or at the extreme of the "cooking and bottling demonstration." They both have their place; but they must be related to our central duty of realizing housewifery as a social function with its tools of work, its raw materials, and its body of consumers.

The other aspect that is worth mention is this. A movement of this nature should have its local habitation, the permanent sign of its existence, the source from which its influence is diffused. It might be suggested briefly that there are three types of establishment we could use for our purpose. One is the obvious shop premises adapted as now for the "food advice centre" service. On the assumption that some of these centres are maintained after the war, it will be necessary to review their work and decide how far they are really worth the cost. The second is the school kitchen, with which a large proportion of our primary schools are apparently to be provided; these kitchens are the concern of the mothers whose children will be fed from them, and they may well become the natural gathering-place, on selected evenings, of many of the housewives of a neighbourhood. The third establishment we might seek to use is the grocer's shop and the dairy. It is true that some educationists would prefer to have their food-teaching uncontaminated by the flavours of commercially retailed bacon and butter. But shops are still a part of our national life; and they are a significant part of the experience of every housewife. If we are to influence popular tastes we must some time begin with the distributive trades, for it is obvious that if we do not draw them into collaboration we may find ourselves competing with them.

Some such course as this will have to be adopted if the wartime experiment in dietetic teaching is not to lapse when the phase of reconstruction is upon us. We have suggested a few reasons for maintaining it in a suitably modified form; and these reasons could theoretically be expressed in financial terms, even though it might be impossible precisely to weigh the saving in hospitalization against the expenditure on public teaching. It is not the business of this essay to decide who shall meet the bill or what the annual dimensions of the bill might be. We are for the moment solely concerned with the conditions necessary for a successful peacetime campaign, for if we do not determine the right conditions before we start we shall spend whatever money we spend to no useful purpose.

A NATIONAL DENTAL SERVICE

TEVIOT COMMITTEE'S RECOMMENDATIONS

The White Paper on a National Health Service said that there must be some temporary exceptions to the comprehensiveness of the service, and dentistry was mentioned as the first of these, owing to the insufficient numbers of dentists to serve the whole population. The Interdepartmental Committee on Dentistry, which has been dealing with the question of adequacy among other matters, has now issued an interim report.[1] The committee was set up in the early part of 1943 under the chairmanship of Lord Teviot, and consists of twenty members, one-half of whom hold a dental qualification. Its outstanding recommendations are:

(1) The setting up of a comprehensive dental service to form an integral part of, and to operate simultaneously with, the National Health Service.

(2) A general dental practitioner service analogous to the proposed general medical practitioner service in the Government scheme.

(3) Experimental dental health centres in suitable areas.

(4) A special effort to improve the teeth of expectant and nursing mothers, children, and adolescents.

Dental Man-power

Some 15,000 dentists are at present on the *Register*, but owing to the large admission of bona-fide dentists at the time of the Act of 1921 the *Register* is at present heavily overweighted in the higher age groups, and during the next few years there will be a rapid loss of names by retirement. The average annual admission to the profession in recent pre-war years was 340, but during the war years the annual student entry has fallen to below 300, and 10% of students, for one reason or another, do not become dentists. These figures are not nearly sufficient to maintain the *Register* even at its present strength. An actuarial table is appended to the report showing that if the number entering the profession annually were raised to 400 in the years immediately ahead, and later to 425, it would still be 30 years before the present effective total number of the profession would be increased. "This," says the committee, "is an alarming forecast."

At present the career of dentistry is relatively unattractive to young people in comparison with other professions, especially medicine. The work is apt to appear unpleasant and its scope restricted, at all events until the scientific interest of it begins to be appreciated, and there is not much opportunity for specialization. There are five dental schools in London, seven in the English Provinces, three in Scotland, one in Northern Ireland, and four in Eire. Some of the schools, like the English provincial ones, are closely associated with universities; others, like the London schools, with hospitals.

Dental Needs and the Present Services

The report says bluntly that "the state of dental health of our population is bad, and its effect on their general health is bad." An average of 90% of the male recruits to the Army in the present war needed dental treatment on enlistment. Of a group of 10,000 Scottish five-year-old children, only 1,000 were found free from dental caries. One approved society in one year found that 12.2% of young persons between 16 and 19 who applied for treatment needed full upper and lower dentures.

In the last pre-war year about 3½ million elementary-school children in England and Wales were dentally inspected; some 2½ million were recorded as requiring treatment, and about 1,600,000 had some treatment. The majority of local authorities, as part of their maternity and child welfare services, make some provision—in most cases meagre—for dental attention. Dentistry is an additional benefit under National Health Insurance, and roughly two-thirds of insured persons are entitled to it, but only 800,000 (less than 7%) claim it on the average each year. "It is a common experience in insurance dentistry that people do not resort to treatment until a stage when the teeth are unsaveable, and then there is gross oral sepsis."

The broad picture of the present position is of a number of public dental services not closely related, and each with shortcomings, and of a public ill educated and apathetic in regard to the care of the teeth. The committee believes that fear of pain and lack of understanding of the importance of dental health are more effective deterrents than the economic factor.

Steps towards an Adequate Service

In making its recommendations the Teviot Committee distinguishes between the *need* for treatment and the *demand* for treatment. If the demand for treatment rose to somewhere near equality with the need there would obviously be a shortage of dentists. It must be the object of policy to increase demand in this way, but the whole question of the shortage of dentists turns upon the probable pace of increase in demand and supply.

"If, for example, a total annual demand rate of the order of 10% to 20% were the experience in the next few years, and if vigorous measures were taken to make the career of dentistry attractive, we foresee no substantial shortage. If, on the other hand, the annual demand rate rose rapidly to 40% or 50% and the numbers of the profession showed no rapid increase, the shortage would be very serious."

The committee urges the acceptance of the principle of a comprehensive service, one which, while not wholly adequate, will be equally available to all who demand it, and will be paid for by the community as a whole. It regards dentistry as an integral part of the comprehensive health service, a fact which in itself, with the prospect of plenty of work, adequate pay, good conditions of service, and the knowledge that dentistry was making an essential contribution to national health, would encourage the recruitment of young men and women to the profession.

The sharpest point in the mobilization of dental forces should be the dental care of expectant and nursing mothers, children, and adolescents. The committee looks for a large expansion of dental services available to school-children (under Section 48 of the new Education Act) as one of the essential foundations of a comprehensive service. It also hopes that employers will give their workers, particularly adolescents, time off without loss of pay for dental treatment.

Fundamental points in any new comprehensive public dental service will include the following:

(1) No compulsion on any dentist to enter the public service.

(2) Any dentist should be free to engage, either whole-time or part-time, in the service or any branch of it in which there is opportunity to serve.

(3) A patient must have free choice of dentist and liberty to alter his choice if he so desires.

(4) The proposals are not intended to interfere with the free right of everybody to seek dental advice and care through private arrangements and by private fee.

Family Dentists: Health Centres

The idea of a general dental practitioner service, analogous to the general medical practitioner service, available to all who wish to use it, and set up on the basis of the family, is put forward in the report. The idea of the family dentist is as yet unfamiliar to a large part of the population; the committee thinks it should be developed and encouraged.

The setting up in suitable localities of dental health centres, providing facilities for team work, is recommended. These centres should be experimental, and the profession should be consulted as to their development, size, siting, internal arrangement, design, and equipment. There must be no compulsion on dentists to work in such centres or on patients to receive their dental treatment in them.

Finally, there are some recommendations on dental health education. The most important factor in such education will be the quality of the treatment given. The dental health centre

[1] London: H.M. Stationery Office. (6d.)

would offer, by means of lectures, films, and the like, opportunities for enlightening the public. "We do not wish to separate dental from general health education; the one is a sentence on the page of the other. But we are anxious that the sentence should not be crowded out; rather than that, we would have it given a page to itself."

Recommendations for securing an increased entry into the profession will be dealt with in the final report. Here the committee urges only the encouragement of ex-Service men and women to offer themselves for dentistry, and the early release of dental teachers from the Forces to resume their work in the schools.

SEVENTH ADDENDUM TO THE BRITISH PHARMACOPOEIA

The General Medical Council will publish on Feb. 1, 1945, a Seventh Addendum to the *British Pharmacopoeia*, 1932, in which new monographs, and modifications of existing monographs, will be included. Arrangements have been made for a limited number of advance proofs to be available, on application, to manufacturers of the preparations described therein, in order that facilities may be provided for the supply of substances in accordance with the new specifications, as soon as they become official.

The following new monographs will be included:

Amethocainae Hydrochloridum
Amphetamina
Amphetaminae Sulphas
Cyclopropanum
Dextrosum Hydratum
Injectio Insulini Protaminati cum Zinco
Liquor Sodii Citratis Anticoagulans
Liquor Sodii Citratis cum Dextroso
Oestradioli Monobenzoas
Oestronum
Pentobarbitonum Solubile
Potassii Sulphas
Progesteronum
Strophanthinum-G
Sulphacetamidum
Sulphacetamidum Solubile
Sulphadiazina
Sulphadiazina Solubilis
Sulphaguanidina
Sulphapyridina
Sulphapyridina Solubilis
Sulphathiazolum
Sulphathiazolum Solubile
Theophyllina cum Aethylenediamina
Thiopentonum Solubile
Unguentum Hydrargyri Ammoniati Aquosum
Unguentum Zinci Oxidi Aquosum

There will also be a general monograph on tablets (including general processes, standards for uniformity of weight, and a disintegration test) and 34 monographs on individual tablets.

The Addendum will contain, in addition, amendments to the *British Pharmacopoeia*, 1932, which have been made official by notice in the London, Edinburgh, Belfast, and Dublin *Gazettes*.

All the official ointments have been reviewed, and a number of revised monographs for ointments are contained in the Seventh Addendum.

The Addendum will contain also new or revised appendices relevant to the monographs in question, and a cumulative index. It must be understood that no additional monograph, or emendation of a monograph, is official until the Seventh Addendum has been published.

SOCIAL BIOLOGY AND THE POPULATION PROBLEM

In a valedictory address from the presidential chair of the British Social Hygiene Council Sir WALTER LANGDON-BROWN discussed social biology in its relation to the population problem.

The family, he said, was the biological unit, and he regarded with grave suspicion the efforts of planners to dethrone the family and to hand children over to the State. The fact that some family life was far from what it ought to be was no reason for destroying something which, in the vast majority, was good. The birth rate had fallen fairly steadily since 1870, and during the same period the infant death rate had decreased and the expectation of life had lengthened. It had been rashly assumed that the level of fertility remained the same, but there were many evidences that the fertility rate decreased with improvement in the chances of survival. The conclusions of a special subcommittee appointed by the British Social Hygiene Council were that one-tenth of all marriages remained childless, though not deliberately so. The great majority of the population did not intend by contraceptive measures to procure permanent barrenness. The subcommittee did not report whether such measures contributed to sterility, and on that question he himself would be non-committal. Medical evidence was accumulating that the one-sided view that if there was barrenness it was the woman who was generally responsible was wrong; from a study of 2,000 marriages it appeared that the defect was on the man's side in 60%, and in general the average male fecundity was much lower than was usually assumed. Couples accepted their fate without generally asking for medical help, though such help was now more effective than formerly, owing to new knowledge.

Turning to other factors operating against the family Sir Walter Langdon-Brown said that he was impressed by the rise in rents which had taken place since the turn of the century. The Victorian rule was that not more than one-sixth of income should be spent on rent, and that at a time when rates were low and income tax negligible. The proportion of total income which went in rent and rates in these days was alarming in its repercussion on family life and on infant mortality, for money was spent on housing which should go on food. The aggregation of urban populations led to the increase of flats, which were an unsuitable environment for children. Decentralization of industry offered some solution, but the real trouble was that building costs had increased so greatly that it was impossible for suitable houses to be made available at an economic rent. Thus there was resort to subsidies, the limit of which might be approaching. The Victorian principle was that everything should be self-supporting so far as possible, but there was danger also in the modern view that nothing need be self-supporting. Family allowances were proposed as an extension of social service, but he could not believe that a standard flat rate would prove satisfactory. It would be of small value except to those at the lowest income level, while those at a higher level would be more heavily taxed in consequence, and therefore might be inclined to limit their families still further. The social changes which compelled later marriages must be recognized. Celibacy was enforced for longer or shorter periods upon our young people. The position was difficult and the difficulties would increase as a result of the toll taken by war. There was scope here for study by the social biologist and for the spread of helpful information. Family life in a good home was the best foundation on which to build the new world.

Dr. Otto May proposed and Dr. Letitia Fairfield seconded a vote of thanks to Sir Walter Langdon-Brown, and the meeting proceeded to elect Prof. F. A. E. Crew of Edinburgh as the incoming president. Warm tributes were paid to Mrs. Neville-Rolfe for her many years of service as secretary-general, from which she is retiring, and she was made a vice-president. The annual report of the council was adopted on the motion of Sir George Elliston, seconded by Mr. McAdam Eccles.

Reports of Societies

TREATMENT OF DUODENAL ULCER

At a meeting of the Section of Surgery of the R.S.M. on Nov. 1 Sir JAMES WALTON, the president, opened a discussion on the treatment of duodenal ulcer by saying there was some danger to-day of going back to the mediaeval concept of authority and accepting the written word instead of the Hunterian notion of research and experiment. The young surgeon, while making himself familiar with Continental literature, should beware of thinking that what was stated there about duodenal ulcer, for example, necessarily applied to cases seen in this country. There was only one indication for surgical treatment—namely, failure of medical treatment; but this varied with the social condition of the patient. A well-to-do man, living a sheltered life and able to diet carefully, was obviously different from the labourer in respect to treatment. In this country the operative procedure for duodenal ulcer had varied between posterior gastro-enterostomy and partial gastrectomy. He still regarded the former as the ideal operation, and reserved the latter for cases which had developed gastro-jejunal ulcer, trying to judge beforehand in which this was likely to arise. For partial gastrectomy his present choice was Billroth I, which he thought less apt to cause immediate disturbance to the patient. To-day the use of the drainage tube was being decried; he had never known it to cause trouble.

Mr. C. JENNINGS MARSHALL said that duodenal ulcer was primarily a condition for medical treatment; surgery was indicated only in certain cases. But the number of medical regimes—all successful, in most cases, until the next time—should lead one to the common factor—rest in bed. Medicines and diets were directed to reducing the "acid in the stomach," but hydrochloric acid digested nothing, and any excess above 0.08% resulted in no increase of peptic activation. If it were conceded that the gastric secretion was, in part at any rate, responsible for the ulceration, at least it was to be urged that for prognosis and diagnosis a coefficient of

peptic activity should be noted, not of HCl. While there was some rough parallelism, yet some of the largest gastric ulcers might be associated with a low HCl secretion, even with achlorhydria, but apart from that there was reason for regarding high secretory activity as secondary to peptic ulceration, not causative.

With or without treatment 80 to 85% of cases of duodenal ulcer did not need surgery, and roughly one-sixth developed either imperative indications or progressed slowly to chronic invalidism or economic crippling. Perforation called for surgery, and so did recurrent massive haemorrhage ; but apart from these cases there were others which from the first relapsed rapidly after the most stringent medical treatment, and there were the chronic slowly progressive ulcers which produced increasing economic invalidism. As for choice and results of operation, in 250 resections for duodenal ulcer there had been 7 deaths. In 35 resections for gastro-jejunal ulceration there had been 4 deaths. Of 350 gastro-enterostomies, done largely in the pre-gastrectomy era, about half the cases had been traced or reported, and two-thirds of these were free from serious symptoms. He had seen no serious case of anaemia follow resection.

Medical Treatment

Dr. HORACE EVANS said that in most cases the diagnosis of duodenal ulcer was fairly easy. The history was typical and *x*-ray confirmation made the diagnosis complete. But sometimes the history was difficult, particularly in women. One point was the frequency with which complications such as haemorrhage, perforation, and even stenosis might occur with minimal dyspeptic symptoms. In the more acute superficial ulcers, very shortly after the haemorrhage, no trace of the ulcer might be demonstrable radiologically. Much time and labour were wasted on test meals—of real value only in cases of obscure anaemias, some cases of carcinoma of the stomach, and cases of chronic gastritis.

The speaker had been impressed by certain aspects of medical treatment. Satisfactory healing was unusual if the patient was ambulant. There should be a minimum period of six weeks' rest in bed, followed by a further six weeks' quiet period. Mental relaxation was as important as physical, and sedatives were more important in the healing of the ulcer than alkalis. To suppose that alkalis formed a soothing lining in the stomach and duodenum and maintained a lower acid content was fantastic. In the feeding of the patient the nature of the feeds mattered little as compared with their frequency. Sometimes harm was done by too strict a dietetic regime. In hospital the results of treatment of these patients in special gastric wards with a proper regime and exclusion of unsuitable foods had justified itself. If the need for surgery did arise, certain often neglected points should be stressed. Preoperatively the state of the lungs should be ascertained, not only by clinical but by *x*-ray examination, and the question whether the patient was anaemic or not was also important.

Sir HENRY TIDY felt that peptic ulcer on the Continent was not the same as in this country. Indeed, geography was a factor in all assessment. The incidence of gastric and duodenal ulcer—both total incidence and the incidence of the one as compared with the other—was entirely different in Scotland from what it was in London, both being far commoner in Scotland. Duodenal ulcer was extremely common in South India but almost unknown in North. He suggested that most gastric ulcers which began in early life were cured, disappeared, and did not recur. Duodenal ulcers followed a different pattern. Gastric ulcer increased enormously all over England between 1920 and 1930, but the incidence of duodenal ulcer during the same period actually fell. Both surgeons and physicians agreed on the necessity for rest in bed—and that was the first thing the surgeon ensured by his operation. Medical treatment was much easier to repeat than surgical treatment, and with it there were better results the second time the patient was treated than the first.

Types of Duodenal Ulcer

Major-Gen. W. H. OGILVIE confessed himself "distressed" to hear Mr. Jennings Marshall allude to "peptic ulcer." He thought that the distinction between gastric and duodenal ulcer was an established one. They were two distinct diseases. It might almost be said that in duodenal ulcer they were dealing not with one disease but with one of three—duodenal ulcer A, B, and C. Duodenal ulcer A should be left to the physician so far as possible. It was associated with rapid emptying and high acidity. The patient was likely to be a "go-getter," of worrying temperament, and a cigarette smoker. Duodenal ulcer B was the ulcer which perforated and was practically never chronic (chronic ulcer did not perforate). The patient might be a healthy workman in full work and perfectly well until 48 hours beforehand. Many of these cases showed no further trouble. Duodenal ulcer C was an ulcer which bled—meaning by bleeding, catastrophic haemorrhage. The history was a silent one, not a duodenal ulcer history. This was a disease of "better-off" and of rather older people. Such an ulcer was an indication for surgery. The mortality after one attack was about 8 to 10%, and if the group were followed up the eventual mortality might be found to be very much higher.

Prof. C. A. PANNETT contested Major-Gen. Ogilvie's statement that duodenal ulcer A was a medical disease. There were numbers of patients treated medically whose life was a misery from constant pain. He did not think a treatment was worth anything if it had to be carried on for the rest of the patient's life. Undoubtedly medical treatment cured a number of ulcers permanently, but he did not think a man who had to take alkalis rapidly and continuously could be said to be cured of his ulcer. Yet in such cases surgery would bring about an absolute cure. His own standard of cure was that a man should go away and at least within three months be able to eat anything and within a year to eat normal-sized meals without having to think about them.

Mr. HERMON TAYLOR spoke of the man who got steadily worse after having conservative treatment for many years. What was the surgeon to do? The choice between partial gastrectomy and gastro-enterostomy was one on which there was a division of responsible opinion. He had set to work on some of the intractable cases of dyspepsia in which the operation of gastro-enterostomy had failed. All patients with duodenal ulcer had a marked excess of folding in the gastric mucosa. The late Sir Arthur Hurst had pointed out that the degree of rugosity in the stomach was a congenital characteristic. This seemed to him a rational explanation of the varying response of patients with duodenal ulcer to gastro-enterostomy. It appeared that gastro-enterostomy was sufficient to cure a duodenal ulcer provided there was not too great an excess of gastric secreting area, but if there was a gross excess then the patient was worse off than before and got a gastro-jejunal ulcer. In cases in which there was an excess of folding a partial gastrectomy should be done. No severe operation was justifiable if a less hazardous one would cure the patient. There was no comparison between the risk of gastro-enterostomy and of partial gastrectomy, and the latter should never be done unless it was "the only way."

Mr. G. W. BERESFORD said that apart from rest there was nothing one could do which could be called medical treatment. The most satisfactory operation for chronic duodenal ulcer was a subtotal gastrectomy. He repeatedly saw cases in which gastro-enterostomy had been done which not only developed gastro-jejunal ulcer but years afterwards got recurrent duodenal ulcer. Dr. J. J. SPIRA mentioned the treatment of chronic peptic ulcer on a low-fat diet. Mr. HAROLD DODD said that in the few cases in which he had carried Somerville's operation out the functional result was good, though the fractional test-meal showed no difference. He had not found from his follow-up that any more patients developed anaemia after partial gastrectomy than after gastro-enterostomy.

At a special general meeting of the Royal Academy of Medicine in Ireland, held in the Hall of the Royal College of Physicians of Ireland on Nov. 24, Mr. A. A. McConnell, F.R.C.S.I., was elected President of the Academy.

E. P. Scott and A. B. Ortner (*Amer. J. Dis. Child.*, 1944, **68**, 118) report a case of typhoid fever in a boy aged 11 years who survived successive multiple intestinal perforations. They appear to be a "record."

Correspondence

Time of Ovulation

SIR,—I appreciated the admirable annotation on ovulation and fertilization which appeared in your issue of Oct. 21 (p. 537). The facts as stated in this note have been substantiated by the majority of embryologists working on early human development. The letter by Prof. F. Davies of Sheffield, which appeared in your issue of Nov. 18 (p. 671), calls for some comment. The menstrual history of the patient, from whom the 9–10-day embryo was secured, is apparently the crucial point on which he bases his conclusions as to the time of ovulation. Even, however, on the assumption that ovulation occurred on the ninth or tenth day of this cycle, there is no evidence that the cycle, if uninterrupted by pregnancy, would have been a 28-day one. In fact, Prof. Davies, in his article with Harding (*J. Obstet. Gynaec. Brit. Emp.*, 1944, **51**, 225), states:

"It is noteworthy that the histological structure of the endometrium on the 20th day of the cycle in the present case is closely similar to that of the endometrium on the 24th or 25th day of a 28-day cycle in a number of specimens examined by the present authors, and it is certainly much more advanced in the secretory phase than many 20-day specimens examined from women with 28-day cycles; in these cases ovulation probably occurred about the 14th day."

These changes in the endometrium, which are in agreement with the findings of Rock and Hertig (*Amer. J. Obstet. Gynec.*, 1942, **44**, 973; 1944, **47**, 343), point clearly, in my opinion, to the conclusion that the relevant cycle of the case described by Prof. Davies, had it been completed, would have been of about 24 days. This, of course, would mean that ovulation occurred at the time indicated by the writer of your annotation. Prof. Davies, in support of his thesis, then refers to five ova, described by Miller, Engel, and Reimann (*Growth*, 1938, **2**, 381) and Reimann and Miller (*Arch. Pathol.*, 1939, **27**, 412), and states: "All five of these ova indicated that ovulation occurred 15 to 17 days before the onset of the next menses in these 28-day-cycle cases. . . ."

The facts concerning three ova of this series, on which data are presented, are as follows: The first specimen was recovered on the fifteenth day of a cycle the length of which is not stated. In one ovary there was a fresh corpus haemorrhagicum "which on section proved to be a very young corpus haemorrhagicum in which no lutein cells had as yet been differentiated." The second specimen was recovered on the sixteenth day of the cycle; the previous cycles of this patient were of the 28-day type. This ovum was thought to be one day older than the first specimen. The third specimen was recovered on the fifteenth day after the onset of the last period; the previous cycles were of an average 28-day type. Section of the corpus haemorrhagicum showed a considerable amount of blood and a few differentiated lutein cells. For their investigations Miller *et al.* used 24 operative specimens. These authors state:

"Judging from the experience with these 24 specimens, excluding the 21-day ovum, the periods of the cycle during which the best chances are present of finding an ovum in the tube are between the fourteenth and the sixteenth day after the onset of the previous menses. The ovum recovered on the twenty-first day was degenerated and apparently had been withheld in the tube, since the tube was tortuous and offered resistance to the passage of the wash fluid. We believe the ova entered the tube on the fourteenth day after the last menses, assuming that ovulation took place at the same time in all three individuals. This is the obvious conclusion for two reasons. Specimens removed on the thirteenth day failed to yield ova. . . ."

It is true, however, that in the summary of their paper in *Growth* these authors state:

"Judging from the days during which these and other ova were recovered the ovulatory period is between the eleventh and thirteenth day after the onset of the previous menses in 28-day-cycle cases." In my opinion this statement is not borne out by their own findings. Finally they state:

"Probably the earliest day that the ovum can be found in the Fallopian tubes is the fourteenth day after the onset of the last menses." This of course would mean that the ovum takes several days to reach the tube after ovulation—which seems most unlikely.

It may be of interest to add that I have recently recovered two further ova: one, at the pro-nuclear stage, on the seventeenth day of a cycle of the 28-day type; the other, an abnormally segmented egg, on the eighteenth day of a cycle of the 28-day type. It is probable that the first specimen is about 48 hours and the second specimen is about 72 hours old.—I am, etc.,

Anatomy Department, St. Bartholomew's Hospital Medical College. W. J. HAMILTON.

The Nursing of Tuberculosis

SIR,—Your annotation on the nursing of tuberculosis (Oct. 28, p. 569) calls for comment. Quoting the combined report of the Joint Tuberculosis Council and the Tuberculosis Association, you state that the risk to sanatorium nurses of acquiring tuberculosis is no higher than that to which general hospital nurses are subject. The important recently published work of Daniels, the Prophit scholar (*Lancet*, Aug. 5 and 12), on primary tuberculous infection in general hospital nurses shows that this risk is not inconsiderable, and he makes the specific recommendation that Mantoux-negative nurses are not to be allowed to work in tuberculosis wards. He shows that of 42 nurses initially Mantoux-negative, 33 developed tuberculosis, as compared with 2,120 Mantoux-positive, among whom 43 developed tuberculosis.

In view of this much higher observed incidence of tuberculosis in Mantoux-negative nurses in general hospitals it would seem probable that the same finding is likely to apply in sanatoria. A small series of figures from the tuberculosis hospital with which I am associated tends to support this view. During the past few years some 30 probationer nurses have been received for three months' training in tuberculosis. Of approximately 189 Mantoux-positive on arrival, 1 has subsequently developed tuberculosis, and of 32 negative, 4 have developed tuberculosis demanding institutional treatment. In addition, of the 32 approximately 25 became Mantoux-positive during their three-months stay. (I write from memory as I have not at the moment access to the figures, which are, however, substantially correct.) These figures, which are admittedly too small to be of statistical value, are, at any rate, suggestive, and I have as a result terminated the experiment and no longer allow Mantoux-negative nurses in tuberculosis wards.

Admittedly sanatoria have and usually exercise their facilities for Mantoux testing, radiographing, and "keeping nurses under observation," but none of these procedures will prevent the nurse from being infected during her work. To know that a nurse is Mantoux-negative is valueless unless that knowledge is applied by removing her from the tuberculous environment. The report as quoted by you states that a nurse of 18 runs no more risk of acquiring tuberculosis than one of 21; agreed, but only if she is Mantoux-positive, which is rather less probable.

In short, it is unfair to the individual Mantoux-negative nurse to expose her to the risk of acquiring tuberculosis; nor will the admittedly difficult problem of staffing tuberculosis institutions be solved by converting with certainty a proportion of Mantoux-negative nurses into tuberculous patients.—I am, etc.,

Abergele, N. Wales. W. E. SNELL.

Endotracheal Connexions

SIR,—At a thyroidectomy recently I was administering nitrous oxide and oxygen through an orotracheal tube when the Magill connexion became detached from the tube. The patient's face was covered with a sterile square, and it was a few moments before I discovered what had happened. In these few seconds the tube had worked itself down quite a few inches, in spite of a pharyngeal pack, and was astonishingly near the glottis before I rescued it. Since then I have had a small hole bored through each side of all my Magill and Rowbotham connexions, and after inserting the connexion in the tube I put a safety-pin through the tube and through the holes, transfixing both tube and connexion. This makes the union quite secure. The hole must not be too small, or it will be difficult to find when it is hidden inside the tube. From experience I have found that if the holes are about 2 mm. in diameter and are placed about 1 cm. from the distal end of the connexion no difficulty is likely to occur in transfixing them.

I have found this very useful in the case of the new vinyl-plastic tubes, which do not hold a metal connexion very securely when they are soft after boiling. Apropos the vinyl-plastic tubes, I find them delightful for oral intubation, and I think they are kinder to the tissues than the rubber ones. I have found, for instance, that after the operation is over and the tube is withdrawn, the end which has been in the trachea is quite soft and flabby with the heat of the body, and I believe it will be less likely to cause tracheal irritation than the harder rubber tube. For nasal intubation it seems less useful. It is a little hard and rigid, unless boiled immediately before use, and then it becomes too soft and loses its curve. It certainly passes through the nose very easily then, but blind intubation is less likely to be successful. I hope the makers will be able to produce one with less rigid walls for nasal use.—I am, etc.,

Edinburgh. A. MCCALLUM MILLAR.

Artificial Respiration

SIR,—Surely the first essential in the treatment of respiratory arrest is to ensure that the resultant anoxia is counteracted without delay. Normally the chief function of respiration is the oxygenation of the blood; if the patient stops breathing for himself the obvious and most imperative remedy is for someone else to do it for him.

The first thing to be done is to make sure that the airway is clear; this point is often forgotten, not only in the resuscitation of the apparently drowned but even in the ideal conditions of the operating theatre. Next a well-fitting mask, with the expiratory valve closed, should be applied to the patient's face and connected with a breathing bag full of oxygen. If now the airway is kept clear and the bag is squeezed oxygen must be forced into the patient's lungs, and the chest will in fact be seen to expand. Release the pressure on the bag and the recoil of the thorax will cause expiration to take place. Continue the rhythmic contraction and expansion of the rebreathing bag, and so long as the airway is unobstructed and the circulation is adequate, the blood will be completely oxygenated and the patient will suffer no harmful effects of anoxia.

This is the simplest and most effective method of artificial respiration. It is without danger, whereas ribs can easily be broken—and frequently are—by over-energetic measures applied directly to the chest wall, and it has the added attraction that it is considerably less tiring. Then, when all this is done, and then only, should any recourse be had to drugs.

Dr. Bartley (Nov. 11, p. 643) apparently regards artificial respiration as tedious and useless exertion. In the absence of an unobstructed airway, of which he makes no mention, any such exertion is completely useless and therefore bound to be attended by the anxiety which colours his picture. The drugs he mentions will lose none of their power, and will, in fact, probably not be needed if no time is lost in relieving the anoxia first in the simple way I have described.

While discussing analeptic drugs may I correct a false impression of my views on this subject which I find has resulted from the wording of Dr. Thacker Neville's letter (Sept. 23, p. 415)? In this letter he says: "As regards Dr. Roberts's criticism on the use of picrotoxin, in future I shall accept his criticism and use leptazol, which is as active as picrotoxin if given in larger doses than picrotoxin, and is certainly more potent than coramine," thereby creating the impression, as I have discovered in conversation with many scattered readers of the *Journal*, that I recommended the use of leptazol in preference to picrotoxin. Actually in my letter (July 29, p. 161) I made no mention of leptazol: my main contention on that occasion was the same as in this letter—namely, that it is better to ensure that the apnoeic patient is not anoxaemic by the simple method of introducing oxygen to the lungs via an unobstructed airway than to put one's faith in any reputed cardiac or respiratory stimulant drug.—I am, etc.,

London, W.1. F. W. ROBERTS.

Anaesthesia and Shock

SIR,—I have read with interest the article in the *Journal* of Nov. 25 on general anaesthesia in shock by Crooke, Morris, and Bowler. Their conclusion that variations in blood pressure during anaesthesia do not indicate any significant change in the plasma volume or haemoglobin concentration is important, and is an interesting contribution to our knowledge of the conditions associated with operative shock.

I do, however, find myself in disagreement with some of the statements made about anaesthesia. I would deny that the anaesthetic is the most important single factor concerned in the high mortality associated with operations on seriously shocked patients. I think that the anaesthetic matters much less than the way it is given. To get the best results in these cases it is essential that the anaesthetist should be experienced in this type of work, and not only in the administration of anaesthetics but in the uses and abuses of resuscitation and in the judgment of optimum time for surgical intervention. He should have followed his cases through their resuscitation, operation, and recovery, or otherwise in the wards, making full use of his blood-pressure apparatus and notebook. The question of the particular anaesthetic agent which he favours is a minor one. Experience has shown that the skill in the proper use of intravenous therapy is often the determining factor in serious cases. Many a patient has suffered from overdose of fluids, morphine, or heat.

I cannot understand the statement that blood-pressure changes were not found to be related to any particular operative manipulation by the surgeon. My experience is that blood-pressure changes are commonly caused even by a gentle surgeon, particularly in shocked cases. Traction on the parietal peritoneum of the upper abdomen, whether direct or through some other organ, causes an initial fall followed by a smaller rise. Exposure of a large length of bowel outside the abdomen will lower blood pressure. Raising of the kidney bridge or gall-bladder bridge will sometimes influence blood pressure. Heavy retraction of limb muscles will lower blood pressure in the seriously ill patient. I agree that these effects are not so obvious when regional or local analgesia has been used.

In my view resuscitation should not be regarded merely as leading up to surgical operation. The process of resuscitation may be a long one, extending over several days, and the operation and anaesthesia should be a part of the resuscitative process. If operative intervention is well timed it will usually be found that the condition of the patient is better after operation than it was before.

The authors conclude that the chief factors in anaesthetizing shocked patients seem to be: first, the use of a minimal amount of anaesthetic; secondly, the choice of an anaesthetic which stimulates rather than depresses the cardiovascular system; and, thirdly, an adequate amount of oxygen. My chief three factors in anaesthetizing shocked patients would be: first, anaesthetizing them at the right moment in the progress of resuscitation; secondly, maintaining an airway which is absolutely above suspicion; thirdly, in suiting the plane of anaesthesia from minute to minute exactly to the surgical procedure.

I agree that good oxygenation is important, but CO_2 retention, which may be present in spite of good oxygenation, is equally important as a cause of post-operative collapse. Finally, of all the five cases of shock quoted none suffered from injuries of the abdomen, thorax, or airway. It is in these cases where the choice of anaesthetic and technique provides the more interesting problems.—I am, etc.,

Colchester. DOUGLAS CLENDON.

Spinal Analgesia in Penetrating Abdominal Wounds

SIR,—In Major T. Moore's article on underwater blast injuries of the abdomen (Nov. 11, p. 627) there is a statement that cannot be allowed to pass without comment. He writes: "The other death occurred, just as the operation was about to be started, in a short-necked emphysematous patient. A spinal anaesthetic had unfortunately been administered by the Etherington-Wilson technique. It was undoubtedly the cause of death." Since the beginning of the war I have anaesthetized over 350 persons suffering from penetrating wounds of the abdomen, a condition in many ways comparable with that described by Major Moore. My experience confirms the wisdom of the usual advice that spinal analgesia should not in general be used in these cases. It is more than probable that it was the choice of spinal analgesia and not the choice

of the Etherington-Wilson technique that was the cause of death in the case described by Major Moore.

It would be a pity if statements such as that quoted were to bring into disrepute a technique of spinal analgesia that was most carefully evolved by the originator, possesses many advantages, and, when the indications for spinal analgesia are observed, has proved both safe and reliable in many different hands in many thousands of cases.—I am, etc.,

R. BINNING,
Major, R.A.M.C.

Sign for Acute Retrocaecal Appendicitis

SIR,—In the *Medical Annual*, 1944, under the heading "A New Sign in Appendicitis," R. Capurro of Montevideo is quoted as maintaining that whether the inflamed appendix is normally placed, pelvic, or retrocaecal, tenderness can be elicited by deep pressure at a point just internal to and above the anterior superior iliac spine. This sign is not new. I read of it first some twelve years ago as a sign for acute retrocaecal appendicitis. It was attributed to a French surgeon, whose name I have unfortunately forgotten. I have used it since then in some hundreds of cases, and I can vouch for its value in cases of acute retrocaecal appendicitis. In these cases the maximum tenderness will be found just internal to the anterior superior iliac spine; this does not hold for other positions of the appendix. The sign is best elicited by sitting facing the patient, placing the four fingers of each hand over the iliac bones, with the thumbs resting just internal to the anterior superior spines. Gentle pressure with the left thumb will give marked pain in cases of acute retrocaecal appendicitis. In such cases I always use the Rutherford Morison incision, which gives ample exposure. I am sure the sign has a definite value, more especially as the acute retrocaecal appendix is so often missed in its early stages.—I am, etc.,

Warrington. J. J. MANNING.

Treatment by Movement

SIR,—I read with interest Dr. James Cyriax's article in the *Journal* of Sept. 2 (p. 303), and should like to be associated with him in stressing some of the points, at the same time criticizing others. His article deals with:

1. Treatment by movement as soon as possible and choice of type of therapeutic movement, which varies from tissue to tissue, with the nature, position, and extent of lesion, with the integrity or not of such structures as nerve or bone, and with the presence or absence of bacterial infection.
2. Modern methods in the treatment of fractures.
3. The need for deep massage in certain strains of ligaments and muscle attachments working over bone, and in cases of teno-synovitis.
4. The use of passive movement in addition to active movements to maintain or restore full joint movement.
5. The use of faradism only in initial stages.

One of the most difficult problems in treatment of injuries of all types is to know what degree of graduated movement is the right amount for each injury at the stage of recovery in which it is examined. The different types of graduated active movement pass through a sequence of movement from complete rest through gentle movements without weight-lifting to every form of vigorous violent movement. There is no doubt that the A1 soldier requires to be as fit as an international footballer for the duties of modern warfare, and it is not surprising to find that many injured soldiers break down in their training, as their joints are so damaged by the original injury that they are unable to withstand the strain to which they are subjected.

The presence of circulating toxin from some distant focus will naturally interfere with recovery, and in joint injuries, where this is the case, attention may be drawn to it, apart from general and local signs and symptoms, by the following points: (1) The amount of synovitis is out of all proportion to the injury force. (2) The synovium is thickened and spongy. (3) The controlling muscles stutter and twitch on attempting active movement, or when stimulated with faradism. (4) The blood sedimentation rate is raised in some cases, as well as the white cell count. (5) The joint shows failure to respond to exercises and physical treatment by the appearance of recurrent synovitis.

The degree and amount of active movement should vary with each case of injury and should depend on: (1) The amount of traumatic effusion present. (2) The relation of the area of cross-section of the injured structure to the total cross-section of the limb involved. Thus a ligamentous injury taking up a small area of cross-section can be supported, and active movement with weight-bearing or strain started at once, in contrast to a badly sprained joint in which a large portion of the cross-section is involved and in which (3) there is a secreting membrane made sensitive by the injury.

To understand the stages in recovery it is essential to realize that the amount of traumatic effusion can be out of all proportion to the injury, especially if a small vessel is ruptured with the formation sometimes of an enormous haematoma. The natural absorption of haematoma is taking place all the time, but its spread is governed by the following: (1) The forces of gravity either in an upward or downward direction, according to the position of the limb. (2) By the action of the muscles squeezing it towards either their origin or their insertion with the aid of gravity. (3) The direction of fascial planes helped by gravity and muscular action. (4) The direction of venous and lymphatic flow.

I am convinced that, apart from the accurate setting and stabilization of fractures by screws and plates, the excellent results obtained in the early full movement of the neighbouring joints is partly due to evacuation of the haematoma at the time of operation. It would appear to me as a criticism that in cases where screws or plates are employed insufficient understanding in the use of external fixation by plaster was still prevalent. Where a fracture of the tibia and fibula is fixed by a substantial plate and transfixing screws no plaster is necessary. But where screws alone are used in tibial or humeral fractures, or a femur is plated, it is essential for a time to use external fixation by plaster.

I had the opportunity of seeing the results of a few cases of fracture of the femur and tibia treated by the Germans with a long intramedullary hollow metal nail. At the end of 6 to 9 months there was some periosteal bone formation, but naturally little endosteal callus; on removing the nails, however, and applying a spica or long leg plaster, the fracture ends soon consolidated. The nail is introduced through the inner side of the greater trochanter and pushed down the medullary cavity. Another small incision over the fracture allows it to be threaded through the distal fragment, and at the same time fracture haematoma is allowed to escape. By this manœuvre and early knee movement stiff knees were prevented. I consider there may be a definite place for this method in the future treatment of certain fractures of the femur—viz.: (1) introduction of nails; (2) treatment of overlying muscles and neighbouring joints; (3) weight-bearing after 6 weeks; (4) removal of pin at 3 months; (5) plaster-of-Paris walking spica for 2 months.

At the end of six months the femur is firmly united with no knee stiffness. I have been using a method of treating all fractures or injuries with extensive effusion in which open reduction is not indicated by making small longitudinal incisions and thrusting in pointed scissors down to the swelling and allowing drainage or expression of haematoma. Naturally absolute asepsis must be practised, but the results in severe external rotation fracture of the ankle-joint, severe Colles's fracture, and dislocated elbows justify this procedure. It is also combined whenever possible with the cutting of suitable windows for the daily application of faradism, which naturally is combined with active exercises. A more detailed communication on this method is to follow.

I am glad that Dr. Cyriax drew attention to the need for deep massage in certain cases, as the teaching is so much against massage in general that it is often denied to cases in which it should be the main treatment. I would like to add to his list of suitable cases enlargements of infrapatellar pads of fat and collections of organizing haematoma in places where there are no muscles, so-called "dead areas." I am certain that Dr. Cyriax would be first to agree that other forms of physical treatment, such as anodal galvanism, diathermy, heat, and faradism, are a great adjunct to massage.

I am surprised that he uses the phrase "passive movement," and I agree with Watson-Jones that the term should be used only in cases of paralysed muscles. Dr. Mennell has stressed the importance of the range of involuntary movements possessed by each individual joint and how important these movements are for free painless active movement.

Gray's Anatomy describes them as accessory movements and divides them into two types: (1) Certain movements which cannot be performed voluntarily, but only when resistance to active movement is encountered, as in imparting spin to a cricket ball with the fingers, thus causing a rotation at the metacarpo-phalangeal joint.

(2) Movements with complete relaxation of the muscles, as in the play between articular ends of the bones forming a joint.

It is evident then that every mobile joint has a range of (1) active voluntary movement; (2) involuntary movement. These involuntary movements allow for gliding of one bone on the other, rotary movements, and side bending. If after a simple sprain of a joint there are pain and limitation of movement at the end of two months, most orthopaedic surgeons would recommend a manipulation of the joint under anaesthesia, but if gentle manipulative movements are carried out as part of the other treatment, such as exercises, massage, contrast baths, and faradism, it is seldom that there is not a return to full range of joint movement in any sprained joint at the end of three weeks. Therefore I suggest that it would be better to delete the phrase "passive movement" and substitute "gentle manipulative movements." Apart from that, the methods of applying the manipulative movements are quite different, and, as Dr. Mennell points out, passive movements themselves are the cause of inflammatory reactions and increased stiffness, which gentle manipulative movements never produce.

Another important distinction in active movement, which I did not consider he brought out, is the difference between isometric and isotonic movements. With an injured limb in plaster movements will be isometric—i.e., the muscle contracts and broadens, but does not lengthen. As the joint has been placed in the optimum position of rest, movements of this type will prevent wasting of muscles and overstretching of the antigravity muscles, and at the same time hasten the absorption of traumatic effusion. In isotonic movements, although the tone in individual muscle fibres is equal, stretching and alteration in the length of the muscle take place. This may lead to overstretching of one group of muscles with contraction of their antagonistic group. A good wrist-joint and ankle-joint plaster should allow both types of movement, so that the muscles acting on the joint can only move isometrically, whereas, with the wrist and ankle fixed, the fingers and toes can move isotonically. While in plaster the patient must be told that not only must he carry out walking exercises, but he must do each individual movement against the resistance of the plaster so as to bring into use each group of muscles.

Faradism given properly throughout aids and encourages active movement, and allows each muscle of a group to be actively stimulated individually, so that one muscle works on the other, preventing intermuscular adhesions. This is not allowed by active group movement alone, and one only has to see cases treated by exercises plus faradism, compared with those treated by exercises alone, to appreciate the difference in recovery time.—I am, etc.,

W. E. TUCKER,
Major, R.A.M.C.;
Orthopaedic Specialist.

Incidence of Peptic Ulcer

SIR,—In your leading article (Nov. 18, p. 665) you refer to the need for statistics of the total incidence of peptic ulcer in our population. May I suggest that this war has provided a simple means of obtaining such figures? I refer, of course, to the fact that the Ministry of Food has decreed that every sufferer from peptic ulcer is entitled to priority milk and *eggs*. Every food office in the country must be aware of the number of priority forms it has received bearing the figures "Id" (milk) and "I" (eggs): all such forms must indicate patients with peptic ulcers. Surely it would be possible, through the Ministry of Food, to collect such figures and thus determine the total number of peptic-ulcer patients at any given time.

I can think of two possible fallacies: first, that some people who have ulcers have not bothered to obtain their extra milk and eggs (in my experience such a class must be extremely small); secondly, that some doctors may have given to patients without ulcers the necessary forms. Again, I think this must be very rare.

In any case, a very good idea could be obtained of the number of persons in this country who have peptic ulcers sufficiently troublesome to warrant their consulting a doctor.—I am, etc.,

Outwood, near Wakefield. J. D. BOTTOMLEY, M.B.

Sodium Bicarbonate and Peptic Ulcer

SIR,—In view of present-day opinion on the action of sod. bicarb. in stimulating the secretion of HCl, and thus conducing to the formation of peptic ulcer, would it not be wise to omit this ingredient from the tablets magnesium carbonate compound of the *National War Formulary*?—I am, etc.,

Maiden Newton, Dorset. C. LL. LANDER.

Latent Mastoiditis in Infancy

SIR,—May I, as the otologist to the North-Western Hospital, where the possibility of mastoiditis in infants with gastro-enteritis always receives full consideration, make some answer to Mr. Leathart (Nov. 11, p. 637) and some otological comment on Drs. Patterson and Stewart Smith (Nov. 18, p. 659).

In the first place there can be no possible clinical doubt that mastoiditis can play a very important part in the syndrome which we call acute gastro-enteritis of infants. I am not as yet quite sure whether I agree with Mr. Leathart that the disease is a primary mastoiditis, or, more accurately, a primary upper respiratory infection with a secondary gastro-enteritis; or whether there is primarily a virus-produced gastro-enteritis, which, as a result of lowered resistance, allows organisms already present in the upper respiratory tract to become extremely pathogenic. Personally, I incline to the latter theory, but at the moment we have not sufficient evidence to decide one way or another. One can, however, say quite definitely that in a large number of these infants there is a clinically demonstrable upper respiratory infection which most often shows itself as an otitis media, which may or may not proceed to a clinical mastoiditis.

Drs. Patterson and Stewart Smith consider that the diversity of organisms found in the mastoid is a proof that the infection is not a primary condition. That is certainly not a tenable hypothesis. No matter what one's age the organisms found in an acute mastoid can be most varied and can vary in the two ears in the same patient.

Mr. Leathart has done great service in pointing out the three types of bone infection that can be met. My own experience agrees with this, and I have often seen operation on the purely mucoid type followed by an immediate and dramatic improvement. One might add that many a mastoid is passed as uninfected at post-mortem because it only contained mucus and not frank pus. Presumably the mucoid type is only the early stage of an acute infection, brought to the otologist's notice because of our old friends—the virulence of the organism and the resistance of the patient.

I cannot agree that posterior-triangle glands are always an indication for operation. They certainly indicate an otitis media, but I have seen many cases with glands which have recovered without operation. I do not, either, pay much attention to head-rolling, etc.; I prefer to go by the condition and progress of the child taken in conjunction with the aural findings. And it cannot be too strongly emphasized that a gross infection of the mastoid can exist with no more demonstrable lesion of the ear than a loss of the light reflex and a dulling of the tympanic membrane. Hence the necessity for careful and repeated examination of the ears. The appearance of the ears can change completely in a few hours, and the first clinical sign may be sudden dehydration in a child that had previously to all appearances been doing well. It is our rule that no gastro-enteritic baby should be allowed to die—there being no obvious cause for its death—without having its mastoids explored. As I always operate with local analgesia the process is as quick and devoid of risk as possible.

There are some points in the Manchester article which cannot be passed over without comment, as they are definitely misleading. The authors state that under the age of 2 years the mastoids are undeveloped. This is quite untrue. I have seen many completely cellular mastoids at the age of 4 or 5 months, and I am very much inclined to think that an acellular structure at that age is more often an indication of a past infection than of a normal structure.

Subperiosteal abscess is not a common complication in gastro-enteritis; I have never seen it, nor should I have said it occurs commonly in any infantile mastoiditis. Similarly, meningitis is rare. Drs. Patterson and Stewart Smith have rather confused the issue by discussing all infantile post-mortems which showed mastoiditis, whereas Drs. Eiser and Alexander, and Mr. Leathart, have been discussing gastro-enteritis. In this disease the common complications, apart from mastoiditis, are septicaemia (which is usually overlooked), bronchopneumonia, secondary anaemia, and toxic hepatitis. More than one of these conditions can coexist—a fact that has always to be borne in mind. It would seem that all Drs. Patterson and Stewart Smith have shown is the frequency

with which a lethal condition can exist in infants and escape notice. Admittedly, the condition can be most difficult to diagnose. All the more reason, therefore, for it never to be forgotten. The operation table should be the place for infantile mastoiditis and not the post-mortem table.—I am, etc.,

London, W.1. WINIFRED HALL.

Episiotomy

SIR,—Mr. J. D. S. Flew, in his excellent paper on episiotomy (*Journal*, Nov. 11), which deserves widest circulation and attention, suggests calling slight *descent* of the anterior or posterior vaginal wall "vaginal hernia" or "prolapse of the vaginal wall." In my modest opinion this would add another misnomer. Why not call it rightly "*descent*," and that "anterior vaginal wall descent" and "posterior vaginal wall descent" respectively (*descensus vaginae*). More advanced cases should be nominated "*descensus vaginae et vesicae*," whereas still more advanced cases should be called "cystocele" if it is according to the anatomical findings. Applied to the posterior wall the respective names would be "*descensus vaginae et recti*" and "rectocele." Those cases in which the portio uteri appears in the vulva should then be labelled "*descensus uteri*," and the name "*prolapse*" left for those cases in which the uterus (or a part of it) is really *prolapsed*—i.e., fallen out (of the body)—and forms the contents of a bag of the inverted vagina (with or without a part of the bladder).—I am, etc.,

A. W. B.

Artificial Insemination

SIR,—Obviously this new procedure belongs to the same category as birth control and masturbation, both now condoned, even advocated, "in their place." The sexual appetite exists in all or most people; why then, the argument runs, should it not be assuaged "when it becomes too strong to resist"—so long, that is, as any resulting inconveniences to "the community" are fully insured against? Similarly, a woman wants to gratify her "maternal instincts" and have a baby (and the population needs to be increased in view of the ravages of war, of road motor traffic, and so on). Why, then, should she not have a baby if the thing can be done with a minimum of trouble to herself and her husband, he being perhaps incapable or, in any case, uninterested? There are in abundance maternity homes, anaesthetics, crèches, and so forth, and when once her infant, begotten by inoculation, begins to show signs of having a will and personality of its own, and so giving her trouble, the State will take it over and "direct" it into the right paths, while she, the mother, will be relieved of all further responsibility.

As against this facile reasoning, however, comes the awkward fact of the home and the family. This happens to be, *in the nature of things*, the basis of social stability and coherence—the opposite pole from anarchy and chaos. (And alas that our educational authorities themselves nowadays fail to grasp the elementary fact that the home and its surroundings form the young child's natural primary school!)

To say that artificial insemination is justified because it has restored family harmony in such and such a case is exactly like advocating the extended use of opium or alcohol for all the troubles that beset the mind.

Our profession is already suffering badly from competition by the faith healers, patent-medicine makers, and so on. Let it beware lest it lose caste still further by subscribing to this latest doctrine and practice of social disintegration. Man, as distinct from the animals, is provided with brains and an imagination, through which he can transmute his impulses to fine gold.—I am, etc.,

North Queensferry, Fife. A. J. BROCK.

SIR,—Dr. Joan Malleson chides us who condemn artificial insemination for our lack of objectivity and for our appeal to emotion. With respect I suggest that the boot is on the other leg. Dr. Malleson's appeal is on behalf of the woman married to the sterile or impotent husband. In other words, it is a citation of the hard case which notoriously makes bad law, and is essentially emotional. The traditional view of Christendom in regard to marriage and the family is based on a comprehensive objective view of man's whole nature and his weaknesses, and a rational appreciation how the best individuals can best be procreated. Precisely because it regards matrimony as so good it hedges it around with reasonable restrictions: that is what the rational mind does with all good things, and the better a thing is probably the more restrictions in order to prevent the swamping of the best by the less good.

Dr. Malleson's letter is full of appeal to emotion. The spoilt child, in spite of all appeals to reasonableness, nevertheless can only answer, "Yes, but I want to." So Dr. Malleson says of her childless married woman, "Oh, but she wants to." I suggest that rationality does not consist in devising means by which desires condemned by the normal conscience may yet be gratified. Rationality does not suppress emotion and desire, but controls them.

Many experienced practitioners have known cases where a woman who has had herself sterilized on similar emotional grounds has subsequently on cool rational reflection bitterly regretted it. For several millennia women have ministered to men's pleasures and borne children. These two functions have not markedly raised women's status in the eyes of men. The women who have made men sit up and take notice have been those devoted women who have renounced these functions, not because they were bad but because, although so good, still better functions, like the supplying of a mother's place to children lacking a mother, could be pursued. Such super-mothers I have known who excited profound rational respect and admiration. It is not rational but emotional to enthuse over the woman who has a child by artificial insemination.—I am, etc.,

London, N.16. E. H. STRANGE.

SIR,—Recent letters in the *Journal* have argued against artificial insemination on the grounds that it is immoral and contrary to marriage vows.

I feel sure that all rational medical men will agree that it is time the profession as a whole became more far-sighted in its outlook on these matters. This is a changing world, and the things which appear to us most stable, such as human nature and morals, must change inevitably. Authorities tell us that life has existed on this planet for 1,000,000,000 years, and there is no reason to believe that it will not continue to exist for millions of years. Our ancestors 60,000,000 years ago were probably some kind of ape. Millions of years hence our descendants may be as unlike us, physically and mentally, as we are unlike apes. A new moral code will have developed by then to meet the demands of changed conditions. Our conception of marriage will possibly have been completely lost. Of course, in a lifetime one can only hope to see a tendency to change, and this will be recognized only by the more enlightened among us. It should be realized that it is quite futile to fight against this tendency. We can see to-day a tendency for man to take his destiny into his own hands. Artificial insemination is one small expression of this tendency.—I am, etc.,

Hartlebury, Worcs. R. F. STRONGE.

"Dissident Doctors"

SIR,—Dr. Piney's energetic and somewhat emotional response (Nov. 11, p. 640) to Dr. Frederick Dillon's plea (which to me seemed eminently reasonable) for a scientific approach to medico-political problems admirably demonstrates the urgent need for that plea. "It is very odd," says Dr. Piney, "that we doctors . . . should be so easily gulled by the propaganda of authoritarianism." To me it is very odd that he should pay authoritarianism the gratuitous compliment of suggesting that it is the outcome of a scientific approach to politics. It is really rather tragic that at this present juncture the profession, which *should* be the body *par excellence* to advise the nation and its legislature on how to implement their resolve to have a better medical service, should speak with so many voices. The old jibe has it that doctors seldom agree, and one would not need to go beyond the pages of the *Journal* to justify it. Yet the jibe is becoming less and less true in the doctor's professional sphere, where a progressively scientific approach is leading to a rather remarkable agreement of opinion. Surely the inference is clear.

I am sure that Dr. Dillon's view (and Karl Pearson's) is right; but I doubt if his appeal will be heeded by many. The issues will, as heretofore, be determined by a clash of prejudice, and a limited advance, probably in the right direction, will be made. This may be for the best. It will leave the real solution to be worked out *through the scientific approach* by younger and less prejudiced thinkers when these are released from their urgent task of ensuring that human progress is possible at all.—I am, etc.,

Aberdeen. E. R. C. WALKER.

Colonial Medicine

SIR,—The spate of articles, letters, etc., purporting to give pictures of medicine in these long-suffering Colonies of ours continues. May I trespass on the otherwise unsullied pages of the *Journal* to register a further plea, even at the risk of being thought caustic? Might it not be impressed upon intending authors, and then reimpressed upon them, that there are very, very, very few doctors whose opinions are of any interest locally, or of even approximate accuracy, until they have completed about five years of work actually in the West African Colonies? We do not write a history of England after a fortnight at Brighton. No more can doctors write on West African diseases until they have a certain knowledge of the people, some knowledge of the language, and especially some knowledge of the background of family life. Nor is this knowledge acquired from a few months in the coastal belt. Might we not apply the old adage of "Coasters" after seven years, "old Coasters" after fourteen years, to West African medicine, if we substitute "less ignorant" and "more experienced, but more humble" respectively?—I am, etc.,

Colony of the Gambia. J. S. MINETT.

Débridement et Épluchage

SIR,—The use and misuse of these and allied words have already given rise to far too much confusion and misunderstanding.

Débridement is derived from *débrider*, which is the antonym of *brider* (to bridle, to tie up, to fasten, to constrict). *Débrider* is given the following definitions: To incise or slit up[1]; to cut adhesions or tissues which strangle organs (e.g., *débrider une hernie*), or to incise the edges of a wound to provide drainage for pus.[2,3] *Débridement* has nothing to do with debris.

Épluchage is used by very few French writers, the majority using *excision de la plaie* (excision of the wound). It is certainly an error to use *épluchage* for *excision*. *Épluchage* means[1] to peel or pare a fruit, and, used figuratively, to examine or criticize in detail. Moreover, *épluchage* is not given in Garnier and Delamare's dictionary, which is the standard work in France.

Le débridement d'une plaie means the enlargement of a wound, and *excision d'une plaie*, excision of a wound.—I am, etc.,

Leicester. T. M. J. D'OFFAY.

[1] *Harrap's Standard French and English Dictionary*. London, 1934.
[2] *Nouveau Petit Larousse Illustré*, 310th ed. Paris, 1940.
[3] *Dictionnaire des Termes Techniques de Médecine*—M. Garnier et V. Delamare, 12th ed., Paris, 1938.

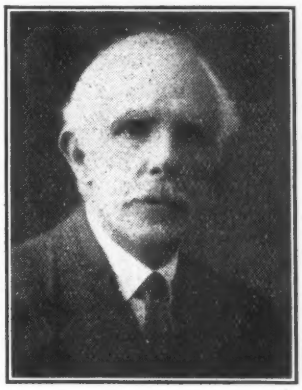
The report of the London School of Hygiene and Tropical Medicine for 1942–3 records a heavy programme of teaching and research successfully carried out. Fourteen courses were attended by 921 medical officers of the British and Allied Forces during the year under review. Shortened courses were also provided for new officers of the Colonial Medical Service, and there was a short course in epidemiology for Polish graduates and senior students. The Ross Institute has continued its work in India, Ceylon, and Kenya, where investigations on onchocerciasis in the East African goldfields are in progress; and arrangements have been made for a helminthological survey in Northern Nigeria. Sir Malcolm Watson has retired from the directorship. Research work undertaken includes experiments on the effect of insecticides on an East African tick, *Ornithodorus moubata;* comparative studies on the digestion and breakdown of haemoglobin in different blood-sucking insects and ticks; and an investigation of the chemistry and biochemistry of patulin. A large number of original papers were published during the year by members of the staff.

Obituary

SIR JOSEPH ARKWRIGHT, M.D., F.R.C.P., F.R.S.

Joseph Arthur Arkwright, who died after a short illness at King's College Hospital on Nov. 22, became an eminent bacteriologist though he did not devote himself to the serious study of bacteriology until he was 40 years of age. During the earlier years of his professional life he was a general practitioner, and the experience gained in the practice of medicine beneficially influenced his subsequent researches.

Born in 1864, he was educated at Wellington, Trinity College, Cambridge, and at St. Bartholomew's Hospital. He graduated M.B., B.Ch. in 1889 and became M.D. in 1895. After serving as house-physician at St. Bartholomew's and the Victoria Hospital for Children at Chelsea and as house-surgeon at the West London Hospital he embarked on private practice in Worcestershire in 1893. Arkwright was a good physician and successful in his practice, but after 10 years he developed an allergy to disinfectants causing an intractable eczema of his hands. This malady was so great a hindrance in general practice that he was obliged to abandon it. As he had a keen interest in natural history he decided to equip himself in bacteriology. To this end he applied to become a private research worker at the Lister Institute. His application was entertained, and in 1905 he joined a small band of research workers, which included A. E. Boycott and John Ledingham, in the bacteriological department under Prof. George Dean. Arkwright soon became a competent bacteriologist, showed a marked aptitude for investigation, and in 1908 was appointed one of the Institute's bacteriologists. He continued to enhance the reputation of the department by his discoveries for nearly thirty years.



In 1915 Arkwright joined the R.A.M.C. and was posted to Malta to take charge of the pathological laboratory of St. George's Military Hospital on the island. Returning to England in 1917 he devoted himself to the study of the aetiology of trench fever. He served on the Commission set up by the War Office to investigate this disease, under the chairmanship of Sir David Bruce, and was responsible for a section of its experimental work. In 1920 he was seconded for one year for special work to the Ministry of Agriculture's Committee on Foot-and-Mouth Disease. In January, 1922, at the request of the Egyptian Government, he went to Egypt with the late Arthur Bacot to make a study of typhus fever and its method of transmission. Both workers contracted the disease and, although his younger companion died, Arkwright recovered from a very severe attack, largely due to the nursing and care he received from his wife, who went to Egypt to nurse him. Returning to England in June, 1922, he was back on duty at the Institute in September of that year. He relinquished his position in 1927. Retirement, however, made little difference to his scientific activity. He retained his laboratory and was made an honorary member of the staff. He enjoyed the feeling that he need not come to the Institute unless he wanted to, but he came just the same. In latter years administration claimed much of his time and energy. He was a member of the Medical Research Council from 1930 to 1933 and of the Agricultural Research Council from 1931 to 1940. In 1926 he was elected to the Fellowship of the Royal Society, serving on the Council from 1931 to 1933, and in 1932 he succeeded Sir David Bruce as the Society's representative on the Governing Body of the Lister Institute. He was proud of this and gave valuable service in helping to guide its destinies. In 1937 he received the honour of knighthood in recognition of his public services.

Arkwright's researches in bacteriology covered a wide range. The best known are those on the variations of bacteria, on the aetiology and transmission of trench fever and of typhus fever, on the physical phenomena concerned in bacterial agglutination, and on immunity to, and the spread of, foot-and-mouth disease. In all these fields of investigation he left his mark, and in the case of the first four he was responsible for the articles on the subject in the *System of Bacteriology* edited by Fildes and Ledingham and published by the Medical Research Council in 1929–31.

In the early days of bacteriology, owing to lack of methods of procuring pure cultures, bacteria were supposed to be capable of extensive variations in morphology and properties. Under the influence of Koch the pendulum swung in the opposite direction, and they were regarded as immutable. The latter view, too, had soon to be modified. Variations in form, colony formation, fermentative powers, agglutinability, and virulence were discovered to occur, even when the culture was made from a single bacterium. Variations could be imposed but sometimes appeared to be spontaneous; some were reversible, others irreversible. Arkwright encountered the phenomenon of variability whilst investigating the properties of meningococci isolated from epidemic and sporadic cases. This was the first piece of bacteriological research upon which he embarked. The phenomenon of bacterial variation fascinated him. He continued to study it for more than 20 years, during which he made some conspicuous contributions to the subject. His chapter on bacterial variation in the *System of Bacteriology* is a scholarly exposition of the knowledge existing at that time by one fully conversant with biological principles.

The researches on trench fever were made when he was a member of the War Office Commission charged with the investigation of this disease. In them he had the advantage of the co-operation of his entomological colleague, Arthur Bacot. Trench fever had been proved to be transmissible by inoculation of a small amount of blood from patients suffering from the disease by McNee and others, and this had been confirmed by the American and British Commissions. Circumstances favoured the view that the infection was louse-borne. A small microbe named *Rickettsia quintana*, less than 1/2000 of a millimetre in diameter, had been discovered in the intestines of lice a few days after feeding upon patients. Microbes of a similar character had been shown to be associated with Rocky Mountain spotted fever and typhus, so that it was conjectured that *Rickettsia quintana* was the cause of trench fever. Arkwright and Bacot confirmed the statements that these small microbes appeared in lice after they had been fed on patients and that lice containing rickettsias could produce trench fever in volunteers upon whom they fed. They found, however, that the surest way to produce infection was to rub the intestinal content of the lice into the lightly scarified skin. The association of the infectivity of lice with the presence of rickettsia was proved by them with the use of lice, fed for many generations on Bacot, of which the intestines were free from rickettsia. As no other pathogenic microbes and no filterable virus could be discovered in infective lice it seemed probable that *Rickettsia quintana* was the causal agent of trench fever. Efforts to cultivate the parasite outside the intestine of the louse were terminated because, after demobilization of the Army, trench fever disappeared. Arkwright therefore transferred his attention to another louse-borne disease, typhus fever, the causation of which seemed also to be due to a rickettsia (*Rickettsia prowazeki*). The study of typhus could not, however, be undertaken in London with the same facility as that of trench fever. There were no cases available and human volunteers could not be used. He had to fall back on animal experiments, and, having obtained lice which had fed on typhus patients in Ireland, infected a monkey in London and passed the disease to other monkeys and to guinea-pigs. He subsequently used these animals for his experiments, but inoculation with material containing the infection of typhus produced only an uncharacteristic febrile illness in monkeys, rats, and guinea-pigs. The association of infectivity with the presence of rickettsias in the lice was found. Experiments on animals with human lice were often frustrated, however, because they didn't live long on a diet of animals' blood and, to keep them alive during the few days required for the rickettsias to multiply in the intestine, Arkwright and Bacot had recourse to rectal feeding of the lice with human blood! To avoid this difficulty, experiments on monkeys were made in which the small monkey louse was used. These told the same story of association between infectivity and the presence of *Rickettsia prowazeki* in the gut of the insect.

The handling of lice carrying the infection of typhus is a dangerous pastime, and a high proportion of research workers doing so have become infected and several have thus lost their lives. This danger did not deter either Arkwright or his intrepid colleague Bacot, and when, in 1922, they received an invitation from the Egyptian Government to investigate typhus fever in Cairo they accepted it with alacrity, as likely to afford them exceptional facilities for carrying on their work. For typhus was endemic there and recovered cases on which to feed their lice were available. They had not proceeded far with the investigation, however, when they both contracted the disease, of which Arthur Bacot died.

Arkwright's contribution to the study of foot-and-mouth disease began in 1920 when the Government decided to permit an investigation to take place in this country. A committee was formed by the Ministry of Agriculture to plan and direct the inquiry, and Arkwright accepted an invitation to join it. He undertook later the direction of part of the researches which it was proposed should be made with the employment of small animals at the Lister Institute. He had a small team to work under him and a suitable experimental animal was available, as guinea-pigs had been recently shown by Waldmann to be susceptible and their infection to be followed by sufficiently characteristic symptoms. Among the subjects on which valuable results were obtained were the plurality of the virus of foot-and-mouth disease in this country, immunity to different varieties, and the possibilities and limitations of enhancing resistance to infection by immunization with vaccines prepared in different ways. The survival of the virus in frozen carcases and other materials, the viricidal action of heat, light, and chemical agents, and the susceptibility of a number of animals which might play a part in distributing the disease were also explored. These researches were published in a series of reports of the committee, and although Arkwright's name appears as joint author of but few of them, they owe much of their success to his inspiration and guidance. In 1931 he succeeded Sir Charles Martin in the chairmanship of the committee. From time to time Arkwright also contributed significant observations on the spread of diphtheria and cerebrospinal fever, and in 1912 he published *The Carrier Problem in Infectious Diseases* with Ledingham as co-author. It presented in readable form the existing knowledge of the part played by the human carrier in the spreading of the six infectious diseases on which the facts are accurately known.

Arkwright was a courteous and kindly person, remarkably modest of his own attainments. He possessed a keen sense of humour and, by his ability to see the humorous side of what were to others irritating occurrences, he avoided quarrels. He was unselfishly good to junior workers with him, and saw to it that they obtained more than their due share of credit for the results of researches inspired, planned, and guided by him. Indeed he possessed the Christian virtues in good measure and was an example to us all.

C. J. M.
H. C.

HENRY BRIGGS, LL.D., F.R.C.S.

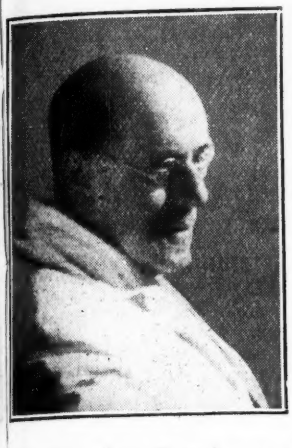
We have to record the death on Nov. 22 at Hoylake, at the age of 88, of Dr. Henry Briggs, for twenty-three years professor of midwifery and gynaecology in the University of Liverpool. To mark his long and valuable service in that chair the university made him emeritus professor in 1921 and conferred on him the honorary degree of LL.D. in 1934.

Henry Briggs, son of James Briggs, was born at Pilkington, Lancashire, and from Manchester Grammar School went to study medicine, first at Owens College and then at the University of Edinburgh, where he graduated M.B., C.M. in 1877. He learned his anatomy under Sir William Turner, winning a senior medal in that subject, and clinical surgery under Lord Lister, winning a medal and first prize. He returned to his native county as demonstrator of anatomy in the Liverpool Medical School, and remained in that city until his retirement from active work. He obtained the F.R.C.S.Eng. diploma in 1884 and lived to become one of the oldest Fellows on the list. His early appointments at the Liverpool Royal Infirmary were those of senior resident medical officer, surgical tutor, and anaesthetist, and he lectured for a time in surgery at University College, Liverpool. From that point onwards he devoted himself to obstetrics and gynaecology, becoming surgeon to the Liverpool Maternity Hospital and to the Liverpool Hospital for Women. In 1898 he was elected professor, and held that post until 1921. He founded a new teaching department in his specialty, and took deep personal interest in the building up of its pathological museum, to which he gave a great many specimens of educational value.

Prof. Briggs joined the British Medical Association in 1878, was an associate member of the North Wales Branch, and presided over the Section of Obstetrics and Gynaecology at the Annual Meeting held in Liverpool in 1912. He was also a past president of the North of England Obstetrical and Gynaecological Society and of the Obstetrical Section of the Royal Society of Medicine. He served for some years on the Central Midwives Board for England and Wales under the chairmanship of Sir Francis Champneys. With Edinburgh he kept in touch by acting as examiner in obstetrics for the university, and the Obstetrical Society of Edinburgh made him an Honorary Fellow. His published writings covered a wide range of subjects in his department.

R. L. RAWLINSON, B.CH.

We regret to record the death of Dr. R. L. Rawlinson, director of the radiological department of the Brompton Hospital. Rupert Lewis Rawlinson was educated at Cambridge and St. George's Hospital, qualifying in 1912. In addition to his appointment at the Brompton, he was honorary radiologist to the Victoria Hospital for Children, medical officer in charge of the electrotherapy department of the Royal National Orthopaedic Hospital, and consultant radiologist to the Ministry of Health. A colleague writes:



The death of Dr. R. L. Rawlinson has deprived us of a great radiologist. His experience was vast and his opinion on a "chest *x*-ray," though always delivered with characteristic modesty, was unrivalled. Many will recall the wise and humorous commentaries which were a feature of his daily sessions in the reporting room. For the past five years, since the outbreak of war, Dr. Rawlinson lived at the Brompton, where he was a much-beloved member of the residents' mess. Those who met him there will always remember his friendliness and his whimsical humour, which, although often shrewd, was never unkind. He was reticent by nature, and only those who knew him well were allowed to glimpse the varied store of knowledge which his unassuming manner so often concealed. As a schoolboy he was interested in natural history, and this remained his chief recreation; he became an expert on alpine rock plants, British moths, and other kindred subjects. In his youth he was a mountaineer of no mean order and he was always a keen fisherman. A kindly, generous man with a great sense of humour, he had an abundant capacity for making friends. The news of his death will bring a sense of personal loss to many generations of old Brompton men, as well as to a host of others who were his comrades.

Medical Notes in Parliament

The Coming Session

On Nov. 28, in the Speech proroguing Parliament that day reference was made to the passage into law during Session 1943–4 of Bills providing for the rehabilitation of disabled persons, the building of houses, and the improvement of water supplies and sewerage in rural areas. The publication of proposals for a national health service and a comprehensive system of national insurance was also recorded.

On Nov. 29 the King opened a new Session. The Speech from the Throne said: "My Government intended that, as opportunity serves, progress should be made with legislation arising out of the proposals already made for a comprehensive health service, an enlarged and unified scheme of national insurance, a new scheme of industrial injury insurance, and a system of family allowances."

Measures embodying proposals for a national water policy were also promised.

During the debate on the Address in reply to the King's Speech Mr. ARTHUR GREENWOOD said many members were disturbed by the relegation of certain proposals to a category of those which should be dealt with "as opportunity serves." It was the House's duty to see that promises which had been made were implemented.

Mr. CHURCHILL said there was no question of postponing a Dissolution to carry legislation which, with the best will in the world, could not be carried this Session.

Sir CHARLES EDWARDS regretted that the King's Speech did not mention the health of the people. The Welsh death rate from tuberculosis was 751 per 1,000,000, which was still too high. The medical officer of health told him that for a hospital in Monmouthshire the waiting period was six months and for Monmouthshire people it was over three months. Children under 5 or of school age were in contact with persons suffering from tuberculosis and awaiting institutional treatment. Of 250 awaiting admission, 42 shared their bedroom with another person.

Manufacture of Penicillin

Mr. GEORGE GRIFFITHS on Nov. 29 raised the question of the manufacture of penicillin in the United Kingdom and the agreement of the British Government with the United States Government concerning it. He said penicillin was closely guarded. Priorities were given to five or six companies. Instead of the British Government taking over the control of the manufacture of insulin they had handed it to the United States and only 5% was made in this country. There was an agreement with the United States that the Forces should have penicillin first. He agreed, but said civilians should have it before German prisoners. In the West Riding County Council laboratory a Czechoslovak doctor had been able to manufacture pure penicillin and lost only 5%, though British manufacturers lost up to 45%. The West Riding County Council could not extend the laboratory and had asked the Ministry of Supply for facilities to do this. The Ministry said the council could continue the manufacture in its own way but must not supply the civil population with penicillin unless they were in West Riding County Council institutions. The council said the Ministry should allow penicillin to be given to anybody where medical officers said it was necessary. This penicillin laboratory was at Wakefield. Penicillin was also made in Bradford and Halifax, but was the "raw stuff" and could only be rubbed into the skin. Was it not time that the monopoly of five firms was ended and that everyone in the country who needed penicillin should be able to get it?

No reply was made by the Government.

Ministry of National Insurance

When the committee stage of the Ministry of Social Insurance Bill was taken on Nov. 14, Mr. PETHERICK moved an amendment to alter the title to that of "Ministry of National Insurance." He said that the name "social insurance" did not mean anything, except that all insurance was to some extent bound up with society. Dr. RUSSELL THOMAS supported the alteration of the title. He said that the word "national" did stimulate some sort of patriotic spirit. He disliked the word "social" immensely because, he believed, it originated in Germany. Mr. Lloyd George borrowed his scheme from the social aspirations of the Germans, but he had the decency to call it "national insurance" when British doctors were going to refuse to work the scheme because of its obvious injustices.

Mr. PEAKE said that the Government included the word "social" because it had been current for many years in international usage. It was a matter, however, for the Committee, and the Government would accept the amendment.

Sir WILLIAM BEVERIDGE said that clearly "social security" was the title in the Atlantic Charter and was understood by people in this country and everywhere as the right title. He opposed the amendment.

The amendment was carried by 170 votes to 80.

Col. ELLIOT moved an amendment to ensure that the close connexion between treatment and payment which existed in Scotland should be continued there. The new steps about to be taken, he said, could be utilized by the existing Minister—the Secretary of State for Scotland. The control of all the great amount of insurance money would pass from Scotland if the Bill went through in its present form. Sir WILLIAM JOWITT, opposing the amendment, said that the object of setting up the Ministry was to make one Minister solely responsible for the various forms of social insurance. If the amendment was accepted a complete division of authority would result. The new Ministry must work on the main principle of devolution. It must decentralize, and leave, so far as possible, Scottish officers sitting in Scotland to deal with Scottish problems with the very minimum of interference from and reference to England. If, for example, an epidemic was breaking out in one of the great cities of England or Scotland, there was at present no means by which the approved societies could communicate with the Ministry of Health. If there were a co-ordinated system of paying sickness benefits on the faith of doctors' certificates, he hoped they would have a Department which would see that these statistics were analysed and checked, so that useful information could be obtained. The Department would be run in collaboration between the Minister of National Insurance and the Secretary of State for Scotland, so that the Ministry of National Insurance could give the Secretary of State what the latter had never been able to have before—the mass of information which came from the payment of sickness benefit, as it must be, on doctors' certificates. It might be that a large number of people in a particular area were getting benefits at a particular time. That

would at once be a pointer, and the medical officer would look into it to see what was the matter. That was something they could not do to-day. The amendment was negatived by 221 votes to 26.

Sir HERBERT WILLIAMS moved an amendment, which, he said, raised the question whether they were going to separate entirely the responsibility for medical benefit from that for cash benefit. The Committee should think before it decided that the right place for medical benefit was outside the scope of the Minister of National Insurance. The Minister should take with him the administration of medical benefit. Dr. MORGAN opposed the amendment. He said that the question of medical benefit was purely a health matter. They could not separate curative and preventive medicine. He wanted to be sure that under the regulations and procedure with regard to medical certification there should be consultation between the two Departments, so that the Minister of National Insurance would not have the power alone to make regulations and decide exactly what medical certification had to be done. The doctors should be free to certify, according to their conscience and their own ideas, within the accepted limits of the ordinary medical procedure with regard to prescribing.

Sir WILLIAM JOWITT said the Government could not accept the amendment. It was desirable that the distinction between medical benefit, which meant medical treatment and assistance, and sickness benefit, which meant periodical payments of sums of money after certification by a doctor, should be drawn in the most emphatic way at the earliest time.

The amendment was withdrawn.

The committee stage was concluded, and the Bill read the third time. Sir William Jowitt said it would be an enormous task to get the Security Bill ready. It was by no means true, as he had heard it said, that it was nearly ready. He would do his utmost to see that no undue time was lost in getting on with the job.

Medical Services in Jamaica

A report is expected shortly from a committee, under the chairmanship of Sir Alexander Russell, which has been set up to review the medical and health position of Jamaica, to consider the reorganization of the administration of the medical and health services, and to make recommendations. No application has reached Col. Stanley from Jamaica for assistance to promote improved medical services.

On Nov. 14 Sir E. GRAHAM-LITTLE asked the Secretary of State for the Colonies whether he was aware that licences to import penicillin into Jamaica had been withheld on the advice of the British Mission in Washington, and what steps he proposed to take to ensure that people in Jamaica might obtain urgently needed supplies. Col. STANLEY replied that licences to import penicillin commercially were doubtless withheld by the Government of Jamaica in accordance with the conditions which had to be imposed in order to ensure that the limited supplies which could be released for civilian purposes were used to the best advantage. Use had to be restricted to centres where adequate facilities existed for controlled clinical trial. To ensure that all supplies reaching the Colony were so used, it was arranged that imports should be through Government channels. As, however, the Jamaica Government encountered some difficulty in obtaining supplies, interim arrangements had been made for an emergency supply to be sent to Jamaica commercially.

Vitamins for Prisoners of War

On Nov. 28 Major MCCALLUM asked the Secretary of State for War whether adequate steps were being taken through the Red Cross authorities to supply to our prisoners of war in Germany, other than those in hospital, the essential requirements in vitamins which were lacking in the low diet afforded by the German Government, particularly now that the supply of Red Cross food parcels had had to be reduced to half a parcel a man a week. Sir JAMES GRIGG said that the composition of the standard food parcels sent out by the British Red Cross Society and Order of St. John was designed and was reviewed by experts in nutrition in relation to the rations issued by the detaining Power. All practicable steps were being taken to restore the normal flow of Red Cross parcels, and it was hoped that the full issue of parcels might be restored shortly. His medical advisers informed him that the reduction in the issue of parcels was unlikely, unless unduly prolonged, to prejudice materially the health of the prisoners. Major MCCALLUM asked if it was a fact that the parcels containing vitamin supplies went only to the men in hospital and not to the men who were not in hospital and who for long years had suffered from lack of vitamins C and D. Sir JAMES GRIGG said that extra vitamins were included in the parcels for sick prisoners, but food sent to the ordinary prisoners contained a supply of vitamins in the normal way.

Release of Medical Student from Navy

On Nov. 28 Sir E. GRAHAM-LITTLE asked the First Lord of the Admiralty if he would consider for release from the Royal Navy a medical student who volunteered for the Royal Navy in 1940 when he had nearly completed his studies for the second examination of the medical degree, but was now anxious to finish his course and assist his father, an overworked medical practitioner, or if he would secure priority of demobilization for this student. Mr. A. V. ALEXANDER replied: No, Sir. I am afraid it is not possible to give any special preference to medical students for release from the Royal Navy. While I appreciate the motives which prompted this young man to join up at a time when he was reserved, there are so many students serving in the armed Forces whose studies have been interrupted by the war that it is not possible to give any of them exceptional treatment. The position has not been overlooked, however, in connexion with the various Government schemes for resettlement and further education.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

Charles Robert Harington, M.A., Ph.D., F.R.S., Director of the National Institute for Medical Research, has been elected an Honorary Fellow of Magdalene College.

At a Congregation held on Nov. 21 the degree of M.D. was conferred upon A. B. MacGregor, G. W. Harris, and I. R. S. Gordon.

UNIVERSITY OF WALES

THE WELSH NATIONAL SCHOOL OF MEDICINE

The following candidates have satisfied the examiners at the examination indicated:

M.B., B.CH.—*Medicine:* Julia P. Gibbs, Sarah M. Lewis, B. H. McCracken, J. E. T. Sobey, M. J. Tanner, J. W. Thomas, P. H. Thomas, W. H. Williams.

SOCIETY OF APOTHECARIES OF LONDON

The Society of Apothecaries of London announces that Brig. Lionel E. H. Whitby will deliver a lecture on "Blood Transfusion in Peace and War" at Apothecaries' Hall, Black Friars Lane, Queen Victoria Street, E.C., on Tuesday, Dec. 19, at 2.30 p.m. Members of the medical profession and senior students are cordially invited.

Applications are invited for the Gillson Scholarship in Pathology, which is awarded for the encouragement of original research in any branch of pathology and is open to candidates under 35 years of age. The scholarship is of the value of £105 per annum. Regulations may be obtained from the Registrar, Apothecaries' Hall, Black Friars Lane, Queen Victoria Street, E.C.4.

Medical News

The Pathological Society of Great Britain and Ireland and the Biochemical Society will hold a joint discussion meeting at the Royal Society of Medicine, 1, Wimpole Street, London, W., on Saturday, Dec. 16, at 11 a.m. The subject for discussion is cancer.

Sir Ambrose Woodall, F.R.C.S., has been given his portrait in oils and a cheque for £500 in recognition of 25 years' service as senior resident surgeon at the Manor House Hospital, Golders Green, London. Mr. A. V. Alexander, First Lord of the Admiralty, who is president of the hospital, made the presentation.

On Nov. 28, after a six-days trial at the Old Bailey, Alva Delbert-Evans, M.B.Toronto, aged 63, with addresses in the West End of London, was found guilty of conspiring with intent to procure abortion, and of having performed illegal operations on two women. William Spencer Lewis, aged 73, described as a surgeon of Staines, Middlesex, and Redcliffe Gardens, Earl's Court, who, with two women defendants, pleaded guilty to conspiring to procure abortion and who also pleaded guilty to using an instrument or other means to procure the miscarriage of six women, asked for thirteen other offences, twelve of which were of a similar kind, to be taken into consideration. In March, 1942, Lewis was sentenced at Surrey Assizes to three years' penal servitude for performing illegal operations on women with intent to procure miscarriage; but after serving fifteen months of that sentence he had been released on a Home Office order on medical grounds, his heart being affected. Mr. Justice Hilbery now sentenced him to three years' penal servitude, saying that but for the defendant's advanced age and infirmity he would have imposed a heavier sentence. He sentenced Dr. Delbert-Evans, who was alleged to have sent women to Lewis for treatment, to five years' penal servitude. One of the two women defendants was sentenced to imprisonment for six months and the other bound over.

A meeting of the Diagnosis Section of the Faculty of Radiologists has been arranged for Friday, Dec. 15, at 2.30 p.m. at 32, Welbeck Street, W., when a paper by Dr. Peter Kerley on the non-tuberculous lesions detected by mass radiography will be followed by discussion. Other radiological meetings to be held about this date are: British Institute of Radiology, 32, Welbeck Street, Dec. 14, 8 p.m., papers on intervertebral disk lesions, and Dec. 15, 5 p.m., medical members' meeting.

Brig. George Macdonald, M.D., D.P.H., D.T.M., has been appointed director of the Ross Institute of Tropical Hygiene, London School of Hygiene and Tropical Medicine, and will take up this post on his release from military service. He studied medicine at the University of Liverpool and has carried out research work on tropical diseases in West Africa and other places. He was appointed assistant director of the Ross Institute in 1939, and joined the R.A.M.C. on the outbreak of war.

The Services

Temp. Acting Surg. Lieut.-Cmdr. C. P. Bailey, R.N.V.R., has been mentioned in dispatches. This name appears in a list of awards for gallantry, skill, determination, and undaunted devotion to duty during the landing of Allied Forces on the coast of Normandy.

Col. J. P. Huban, O.B.E., I.M.S., V.H.S., has been appointed Honorary Surgeon to the King in succession to Major-Gen. H. Stott, C.I.E., O.B.E., I.M.S.(ret.).

CASUALTIES IN THE MEDICAL SERVICES

Killed in action.—Capt. Paul Sabel Adler, Capt. Charles Stewart Ross Lowdon, R.A.M.C.

Previously missing at Arnhem, now officially reported died of wounds.—Capt. Brian Brownscombe, G.M., R.A.M.C.

Previously missing at Arnhem, now officially reported prisoner of war.—Capt. W. I. S. Hudleston, R.A.M.C.

EPIDEMIOLOGICAL NOTES

Discussion of Table

In *England and Wales* notifications of infectious diseases exceeded those of last week by the following figures: measles 249, scarlet fever 203, whooping-cough 113, acute pneumonia 43. There were 103 fewer cases of dysentery, and 23 fewer of diphtheria.

The incidence of scarlet fever in Lancashire went up by 107. Whooping-cough notifications in Yorks West Riding were 44 higher than last week. In contrast to the general trend, Durham reported a rise of 21 in diphtheria notifications. The rise in the incidence of measles, 249, was the smallest recorded for eight weeks. The counties with the greatest increase in this disease during the week were Yorks West Riding 97, Cheshire 96, Staffordshire 88, Devonshire 71, Yorks North Riding 62; a considerable fall was recorded in Lancashire 202, and Southampton 51.

Although dysentery remains at a relatively high level, 217 cases, the total is the smallest for the past fourteen weeks. The chief returns were London 33, Lancashire 27, Essex 23, Yorks West Riding 20, Middlesex 16, Glamorganshire 12, Gloucestershire 11.

Eighteen cases of paratyphoid fever were notified during the week, the largest weekly total since January, 1943. Twelve of these cases occurred in Middlesex, Heston and Isleworth M.B.

In *Scotland* measles notifications fell by 34, diphtheria by 27, and dysentery by 12; those for whooping-cough rose by 19. The largest returns for dysentery were Glasgow 36, Edinburgh 17, Renfrew County 10.

In *Eire* the chief feature of the returns was a rise in whooping-cough from 16 to 60. This disease was mainly notified in three areas: Dublin C.B. 23; Wicklow County, Wicklow U.D. 12, and 14 in the Rural District.

In *Northern Ireland* the high level of measles fell during the week by 16 cases; but the total for scarlet fever went up by 100. Of the 191 cases of measles 187, and 45 of the 90 cases of scarlet fever, were notified in Belfast C.B.

Week Ending November 25

The returns of infectious diseases in England and Wales during the week included: scarlet fever 2,350, whooping-cough 1,388, diphtheria 616, measles 7,137, acute pneumonia 755, cerebrospinal fever 41, dysentery 380, paratyphoid 1, typhoid 4, poliomyelitis 10.

No. 46

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Nov. 18.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1944 (a)	(b)	(c)	(d)	(e)	1943 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	45	3	19	2	2	51	2	26	3	2
Deaths		1	2				1	1		
Diphtheria	619	20	171	110	29	705	40	175	135	27
Deaths	15	—	2	3	1	10	1	3	1	2
Dysentery	217	33	88	—	—	176	49	59	—	7
Deaths				—	—				—	—
Encephalitis lethargica, acute	2	—	2	—	—	2	—	—	—	—
Deaths		—					—			
Erysipelas			62	15	2			50	13	5
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				29					24	
Deaths	55	3	7	8	3	39	1	11	13	2
Measles*	6,001	65	311	34	191	556	49	48	43	3
Deaths	5	—	—	—	—	—	—	—	—	—
Ophthalmia neonatorum	62	6	19	—	—	74	3	20	1	—
Deaths										
Paratyphoid fever	18	1	1 (B)	—	—	4	1	2	—	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal†	626	15	7	4	4	978	73	20	6	1
Deaths (from influenza)	33	1	4	1	—	106	10	32	—	3
Pneumonia, primary			233	26				298	21	
Deaths		38		9	10		48		19	11
Polio-encephalitis, acute	2	—				—	—			
Deaths		—					—			
Poliomyelitis, acute	12	1	2	1	—	8	1	1	1	—
Deaths		—					—			
Puerperal fever		2	12		1		1	18	—	—
Deaths										
Puerperal pyrexia‡	127	8	11	2	1	134	7	13	1	3
Deaths		—					1			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	2,335	56	357	37	90	3,098	258	356	35	90
Deaths	2	—	1	—	—	1	—	—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	7	—	2	13	1	8	—	2	15	2
Deaths	—	—	—	1	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	1,410	46	116	60	13	1,866	151	233	61	20
Deaths	3	1	3	1	—	11	2	2	4	—
Deaths (0–1 year)	366	23	66	30	25	323	37	64	51	31
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	5,099	747	663	184	146	4,934	742	727	228	137
Annual death rate (per 1,000 persons living)			15·2	11·9	§			16·4	15·0	§
Live births	6,507	584	927	337	259	5,562	685	809	284	274
Annual rate per 1,000 persons living			18·9	21·9	§			16·5	18·7	§
Stillbirths	228	18	29			216	27	20		
Rate per 1,000 total births (including stillborn)			30					24		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

‡ Includes puerperal fever for England and Wales and Eire.

§ Owing to evacuation schemes and other movements of population, birth and death rates for Northern Ireland are no longer available.

Letters, Notes, and Answers

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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ANY QUESTIONS?

Some Congenital Malformations

Q.—*What, if anything, is known of the causes of congenital malformations—e.g., cleft palate, talipes, supernumerary digits? What advice on having further children should one give to parents whose history is as follows: Husband aged 38, healthy; wife aged 37, healthy. First child, boy aged 7 years, has right inguinal hernia, flat feet, and a hairy patch of skin on his back. Two miscarriages followed at about 3 months gestation. Fourth pregnancy—a boy now aged 3 years who is healthy but has a slight squint. Fifth pregnancy a girl born 4 weeks premature, died after 12 hours with the above-mentioned congenital malformations. Naturally the parents are anxious to know what are the chances of having a normal child if the wife becomes pregnant again.*

A.—Cleft palate is often inherited, but opinions differ as to the mode of inheritance. It is probably determined by two recessive genes. Talipes equinovarus is inherited as a recessive in some families, but may be due to pressure *in utero*. There are various types of supernumerary digits; the commonest, an extra digit on the ulnar side, is inherited as a recessive, but it also occurs in association with other abnormalities, such as acrocephalosyndactyly. An extra digit on the radial side is usually inherited as a dominant. I do not know an inherited condition in which all these defects occur together. It is unlikely that there is a genetic relationship between any of them and inguinal hernia, flat feet, and a hairy patch on the back which presumably is over the site of a spina bifida occulta, or squint, although all these may be inherited. It is quite impossible to say what the chances are that another child will be normal, but with such a family history I should advise the parents to have no more children.

Threadworms in an Adult

Q.—*A married woman aged 24 with pulmonary tuberculosis has had very severe threadworm infestation which resists usual medical treatment and is unaffected by appendicectomy. The discomfort is so severe that she is losing sleep and weight. Any advice you can give about treatment will be much appreciated.*

A.—Medicinal treatment for threadworm infestation is alone inadequate. The gravid female worms emerge from the anus to lay their innumerable eggs on the external skin, and it is the constant reinfection by swallowing these eggs which is responsible for the maintenance of the infestation. The adult worms live only 2 to 3 months and do not multiply in the gut. The chain of reinfestation must be broken by frequent attention to personal hygiene, and also by rigid precaution against contamination of clothing, towels, bed linen, etc. The use of tight-fitting drawers to prevent scratching and infection of the nails, and of linen which can be boiled daily, will do much to lessen this risk and ultimately to eradicate the infection.

Right Radial Nerve Palsy

Q.—*Shortly after landing in Normandy in June I was confronted, within 10 days, with two cases of right radial nerve palsy. Both men reported that on awakening in their slit trench they were unable to extend the right wrist. On examination, the extensors of the wrist and the brachio-radialis muscle were paralysed, there was tenderness over the musculo-spiral groove of the humerus, and an indefinite area of anaesthesia over the dorsum of the hand. Neither case showed any improvement after several days, so were evacuated. Is this a common condition? What are the pathology, prognosis, and treatment?*

A.—It is almost certain that these men were suffering from a pressure paralysis of the radial nerve, akin to the variety that was said to occur especially on Saturday nights. Usually the nerve does not degenerate and the electrical reactions of the affected muscles remain unchanged (if degeneration has occurred faradic excitability disappears between the 14th and 20th days after injury). Where this is the case the prognosis is excellent and no treatment is required, apart from maintenance of the mobility of the hand. The odd thing is that recovery may be delayed for as long as 5 to 6 weeks: then it progresses rapidly and is ultimately perfect. Recently, Denny Brown of Harvard has shown that the characteristic lesion in this non-degenerative type of paralysis (which the Oxford workers have christened neurapraxia) is a sharply localized demyelination. Perhaps this explains why the motor paralysis is usually more profound than the sensory; the motor fibres are larger and more richly myelinated than those concerned with cutaneous sensibility. And the delay before recovery may perhaps be due to tardy reconstitution of the myelin sheaths. The axons also undergo a histologically demonstrable change, but they do not lose their continuity and there is no true Wallerian degeneration.

It is also just possible that these men were suffering from one form of the obscure neuritis that has appeared from time to time in every theatre of war. The pathology of this condition is unknown and the prognosis is uncertain. But this explanation seems a little unlikely in view of the well-recognized liability to compression of the musculo-spiral nerve and of the fact that these men passed a night in a slit trench.

Regional Ileitis

Q.—*What are the present views on the aetiology and pathology of regional ileitis, or Crohn's disease? What are the symptoms and treatment?*

A.—Though the cause of regional ileitis is unknown, the disease is classified with disorders of the reticulo-endothelial system, since the earliest and most constant change is hyperplasia of the lymphadenoid tissue of the bowel wall and regional lymph nodes. The theories that it is due to tuberculosis or some other infective agent, or that it may be a manifestation of Boeck's sarcoid, are not proven. The cardinal clinical features are abdominal pain, loss of weight, and general debility; the signs of chronic intestinal obstruction; and a palpable mass either in the right iliac fossa or, more usually, in the pelvis. Barium *x*-ray studies show a long filling defect in the terminal ileum—the so-called "string sign." An *x*-ray examination of the chest is essential in making a differential diagnosis. The ideal treatment is primary resection with wide excision of the mesentery. This often means removal of the right side of the colon as well, but it depends on the extent of the oedema and thickening of the bowel wall. In cases complicated by fistula formation the operation may have to be done in stages. The results of excision, both immediate and remote, are excellent. (See Hadfield and Garrod, *Recent Advances in Pathology*; and *St. Bart's Hosp. Rep.*, 1939, **72**, 181).

Local Analgesia for Thoracoplasty

Q.—*What is Magill's modification of Semb's (Stockholm) local anaesthetic technique for thoracoplasty?*

A.—We are not aware that Dr. Magill has published any article under this heading, but the usual technique at the Brompton Chest Hospital (to which he is attached) is briefly as follows. For the first stage (upper) thoracoplasty, after adequate premedication, the patient is placed on his back and supraclavicular brachial plexus block performed, a mixture of 0.5% procaine, 1 in 1,000 amethocaine, with the addition of 1 in 250,000 adrenaline, being used. The patient is then turned on to his sound side and the line of incision is deeply infiltrated with half-strength solution (1 in 2,000 amethocaine and 0.25% procaine). Some of this solution is also injected under the posterior border of the scapula. Posterior thoracic nerve block corresponding with the ribs to be removed can be done at this stage, but is usually left for the surgeon to perform under vision when the flaps are raised. Subcuticular wheals for the reception of the towel clips are then raised. Anterior intercostal block was practised at one time but is now usually omitted as unnecessary. For second-stage thoracoplasty, the brachial plexus block is not required.

Failure to Ovulate

Q.—*Is it a fact that in some women sterility is due to failure to ovulate? Assuming that there is no organic disease of the ovary, what would be the cause of this condition? Is there any means of deciding whether a woman ovulates or not? How can this condition be treated?*

A.—It is an undoubted fact that sterility may be caused by failure to ovulate. As it is not known for certain what causes ovulation to take place it is difficult to say what causes this condition, though it is generally assumed that it is due to some defect or disorder of the anterior lobe of the pituitary. Evidence of ovulation and of corpus luteum formation can be obtained by biopsy of the endometrium during the week preceding menstruation or on the first day of the menstrual period. A sample of the endometrium is easily obtained with a suction curette, and no anaesthetic is needed for this simple operation. After fixing and staining, the endometrium is examined microscopically for evidence of the secretory changes which indicate the presence of an active corpus

luteum. The most important of these is "ferning" of the endometrial glands. It must be remembered that periodic uterine bleeding, simulating menstruation, can occur in the absence of ovulation.

In cases of sterility due to failure of ovulation, an attempt can be made to stimulate the ovaries. Small doses of *x* rays to the pituitary and ovaries have been tried, and some successes have been claimed. Alternatively, some pituitary preparation may be used, and this is the most logical method of treatment in these cases. A new product, which is a combination of follicle-stimulating hormone from the anterior pituitary and luteinizing gonadotrophic hormone from pregnancy urine, has been found to have a profound stimulating effect on the ovaries. Mazer and Ravetz (*Amer. J. Obstet. Gynec.*, 1941, **41**, 474) found that two women out of eight treated with this product for sterility, caused by failure of ovulation, conceived soon after treatment. Great care is necessary in its use owing to its very powerful effect.

Autohaemotherapy for Asthma

Q.—*Why does injecting a patient's own blood intramuscularly have a good effect upon an asthmatic patient? I tried this recently with a tuberculous patient who suffers from asthma, and it did him good.*

A.—Autohaemotherapy and autoserotherapy are on occasion employed in the treatment of allergic skin conditions, especially eczema and urticaria; and usually only in asthmatics who (*a*) resist other forms of treatment, or (*b*) have a cause that is unknown or cannot be determined, and the attacks are thought to arise from substances occurring or manufactured in the body—for example, the treatment of menstrual asthma with serum derived from autogenous blood withdrawn during the premenstrual stage. Any improvement is usually of short duration.

It is thought that the blood in destruction liberates certain substances which on their own or on conjugation with other body proteins act as foreign substances and in some way alter the reactivity of the patient. Others consider that the blood contains the specific allergen and that the systemic administration of the minute quantities of this allergen present in the blood stimulates the production of specific antibodies. Hence it is thought that better results are likely to occur when minute quantities (0.1 c.cm. intracutaneously or 1.0 c.cm. subcutaneously) each 2 days for 12 injections are given than, say, injections 10 to 30 c.cm. intramuscularly once a week. Unfortunately for this suggestion it has been shown that blood or serum derived from a non-allergic person can lead to equal immediate temporary improvement.

With our recent improvements in the determination of and testing for specific causes the number of cases with indeterminable origins lessens and the doubtful temporary beneficial effects of autohaemotherapy are less often sought.

Rammstedt Operation

Q.—*What is the condition found at the junction of the stomach and duodenum some months or years after the Rammstedt operation has been performed?*

A.—The writer's experience of the conditions found at the pylorus some time after a Rammstedt operation is limited to two cases—one three weeks after operation and the other after an interval of six months. In the first the infant died of an attack of D. and V. while still in hospital, and in the second the cause of death was an intercurrent condition; the result of the operation had been excellent. In both, the pyloric region was quite free from adhesions, and the oval scar over the front of the pylorus was very thin and tissue-paper in type. There was, however, no herniation of mucosa. The ridges left by the cut muscular edges could still both be seen and felt. The surprising feature was that the result at the end of three weeks looked almost the same as that after six months, except for a little more smoothing of the edges in the latter. Although I have several cases operated upon over twenty years ago which have since been seen and appear to be in good health, no opportunity has occurred of exposing the exact state of affairs. In one of these cases a barium meal showed some irregularity of the pyloric canal, but not sufficient to enable the condition to be recognized had the previous history not been known.

Senile Softening of Vertebrae

Q.—*A patient, female, aged 69, is suffering pain in the back. X-ray examination shows a senile softening of the vertebrae causing pressure on the nerve roots. Is there any treatment for this condition?*

A.—Senile softening of the vertebrae can be a serious disability in advancing years and treatment is difficult. To promote better calcium assimilation is a primary object, for which purpose irradiation with ultra-violet rays is desirable, combined with the administration of calcium and vitamin D, preferably parenterally, as the oral route is often ineffective in these cases. Support for the spine is essential to prevent the increasing kyphotic tendency, and rest in bed on a firm mattress is desirable as a general principle but is often badly borne by the aged and can then be adopted only for part of the day. A well-fitting spinal brace or corset should be worn when up. For the immediate relief of the pain caused by pressure on the nerve roots injection of procaine, 1% in saline, may be effective, 10 c.cm. or more being injected round the affected nerve roots at their emergence from the spine, and with this may be combined infra-red irradiation and light massage.

X Rays for Herpes

Q.—*What is the value of x rays in the abortion or treatment of herpes?*

A.—Small doses of *x* rays are valuable in the treatment of recurrent herpes simplex, where the same area is constantly involved. They have little or no abortive effect on the actual lesion.

Subcutaneous Swellings

Q.—*A woman aged 61 has for two years suffered from painful swellings of 2 to 5 days' duration in the subcutaneous tissues of hands, wrists, ankles, feet, and sometimes of the thighs, knees, and legs. They are at first small and tense, and then spread to a diameter of 4 to 5 inches. There is no heat or redness. Often one succeeds another rapidly so that the hands are nearly always swollen. Oedema is present at the height of an attack; later there is a soft, tender, ill-defined swelling without oedema. The pain and stiffness cause considerable disability. Sometimes there is slight bluish discoloration at the centre. Occasionally the hands return to normal. Blood pressure 100 mm. systolic B.S.R. 9 mm. in 1 hour. Urine, x-ray of hands, blood count, electrocardiogram, all normal. Haemoglobin 70–85% unless taking iron. The patient, naturally alert and active, is easily fatigued, and is very sensitive to extremes of temperature. The condition followed acute cystitis, which was cured by sulphapyridine. Constipation is extreme, and a colonic irrigation was followed in a few hours by an unusually severe outbreak.*

A.—The attacks are suggestive of sensitization to a foreign protein or a micro-organism. Skin tests should therefore be performed and search made for septic foci. The patient may also be tested for sensitivity to the bacteria present in her mouth, nose and throat, stools, etc. If no specific cause is found, non-specific desensitization may be attempted, preferably with injections of whole blood. The blood is withdrawn from a vein in the arm and injected intramuscularly. It is usual to give a series of six injections at intervals of 5 to 7 days; the amounts injected are 5, 6, 7, 8, 9, and 10 c.cm. A radical change of diet is often successful, particularly a lacto-vegetarian regimen with added lactose or rice-starch to promote an acidophil flora in the stools. Unfortunately this is difficult to manage in wartime. General sedation may also be of value, such as a nightly dose of barbiturate if the patient is not sleeping well.

Water-tolerance Test and Pituitary Function

Q.—*Is a water-tolerance test of much value in estimating pituitary function? Can you give details of the method of applying and interpreting the test?*

A.—The water-tolerance test of Volhard is that most commonly used. The patient drinks one litre of water within one hour in the early morning. During the following four hours he micturates at intervals of half an hour. In health practically the whole litre is excreted within two hours. If a patient does not excrete the whole amount, water retention can be diagnosed but no information is given about the cause of the retention. In most cases it is cardiac or renal. A poor excretion is also shown by many obese patients whose cardiac and renal functions are normal. Signs of endocrine and autonomic imbalance often accompany the obesity in such cases, and it is tempting to postulate a lesion in the diencephalon, where centres regulating water and fat metabolism and pituitary function exist. The whole question of fluid metabolism is, however, still obscure, and in the presence of so many variables it would be unsound to regard Volhard's test as a test of pituitary function.

Penicillin and Disseminated Sclerosis

Q.—*Have therapeutic trials been made on the value of penicillin in disseminated sclerosis? One theory about this disease is that it is due to a spirochaete, against which, presumably, penicillin would be effective.*

A.—We know of no reports on the treatment of disseminated sclerosis with penicillin, either in this country or even in the U.S.A., where clinical research on penicillin has been on a wider scale and included a greater variety of conditions, some rather unpromising. Whether the treatment of disseminated sclerosis has any prospect of success certainly depends on the truth or otherwise of the spirochaetal hypothesis in connexion with this disease, and most will agree that this is rather too slender a thread to support much weight. But everything is worth trying once, and it seems justifiable, if supplies allow, to treat a disease of completely unknown aetiology, always provided that it has characters compatible with an infective origin.

Spread of the Common Cold

Q.—*Is the common cold spread by fomites? What is the risk of infection from making the bed of a person who has a cold, and would it be diminished by wearing a mask?*

A.—It is not possible to give an unequivocal answer to the first part of this question. There is good evidence that the common cold is due to a filterable virus, since men and monkeys have been infected by filtered nasopharyngeal washings from "colded" persons. But artificial cultivation of the virus is extremely difficult, and successful propagation by this means has been claimed by only one team of workers. We are therefore ignorant of the biological properties of the cold virus, including its resistance to natural drying. However, circumstantial evidence suggests that it may survive for a time outside the body. Bliss and Long found that monkeys in strict isolation became infected through food prepared by an individual with a cold. Influenza virus remains viable in the air of a room for some hours and on fabric for some days, so it seems possible that the cold virus will do the same.

Blanket dust has proved to be a source of infection with respiratory bacterial pathogens, and therefore it seems not unlikely—although there is no proof—that an individual inhaling dust from the bed-linen of a "colded" person may become infected in this way. Protection against infection by wearing a mask is possible if the mask is efficient—i.e., it must fit pretty closely to the face and must not allow the passage of fine dust. A mask of the snout design, made of six layers of butter-muslin or of gauze with a 42 by 42-strand mesh largely fulfils these requirements. Repeated laundering improves the efficiency of the mask by narrowing the interstices of the mesh. The transmission of the common cold is very well discussed by Browning in *Control of Common Fevers*.

Scalenus Anticus Syndrome

Q.—*How is the scalenus anticus syndrome diagnosed and treated? How exactly is elevation of the arm for purposes of testing of cervical rib (or other pressure on the subclavian vessels) attempted?*

A.—The term "scalenus anticus syndrome" is misleading. It originated in the United States and was first used for a group of cases presenting the clinical picture of cervical rib but in which no cervical rib could be demonstrated. The application of the words "scalenus anticus" to this group of symptoms was due to the fact that Adson and Coffey (1927) had clearly demonstrated the influence of the scalenus anticus, particularly in the matter of treatment of a typical cervical rib. Tenotomy of this muscle, by giving more room for the brachial plexus, would relieve the symptoms associated with a cervical rib and render excision of the cervical rib unnecessary.

It is rather a pity that Ochsner and his co-workers (1935) used the term "scalenus anticus syndrome," for, as Freiberg (*J. Bone Jt. Surg.*, 1938, **20**, 860) later showed, it has distracted attention from the causal factors of postural relaxation and brachial plexus drag, from traumatic and arthritic lesions of the cervical spine and shoulder girdle, etc. Furthermore, enough notice has not been paid in the United States to the work of Telford and Stopford (*Brit. J. Surg.*, 1919, **7**, 168; 1931, **18**, 557), who have analysed the variations in the lowest trunk of the brachial plexus, the occasional separation beneath it of sympathetic fibres in a separate bundle, and the influence of this upon vascular symptoms distally. Other recent work has shown the important part which cervical intervertebral disk lesions may play in the production of this group of symptoms, which in many ways bears a striking similarity to sciatica. The work of other British neurologists is in this connexion well worth mentioning—e.g., Walshe, in the *Lancet* (1944, **2**, 173).

I therefore prefer not to refer to any such thing as a "scalenus anticus syndrome." There are a variety of symptom complexes related to the brachial plexus and subclavian vessels of which a careful analysis must be made and for which causes must be sought at least as high as the spinal-cord segments concerned. In a downward direction the search should not end at the scalenus anticus or first rib, but should include lesions anywhere in the upper extremity which may fix or lower the shoulder girdle. Certain it is that undue attention to the scalenus anterior muscle may lead to premature surgical attack upon it when more conservative measures may suffice to relieve the patient. It is the same thing, of course, with sciatica, in which knowledge of the influence of intervertebral disk retropulsion has caused many surgeons to lose a sense of proportion.

To say, therefore, what the treatment should be would require a lengthy article and would cover a big field of psychology, orthopaedics, rheumatology, and neurosurgery; and for which a few lines at the end might be devoted to tenotomy of the scalenus anticus, a procedure which may allow a little more room for the constituents of the lowest trunk of the brachial plexus. Elevation of the patient's arm by the examiner should be done with the patient sitting and in recumbency. It is useful to do it in straight abduction and also combined with external rotation of the shoulder of varying degrees, changes in the arterial pressure being estimated by palpation at the wrist or by a sphygmomanometer in the different positions of the limb. Explanation of the changes noted is not always by any means easy, and the possible influence of the clavipectoral fascia and the lower edge of the subclavius muscle in forming an edge, around which nerve and vascular structures may be kinked or by which other disturbances may be aggravated, should not be overlooked.

LETTERS, NOTES, ETC.

New Houses

Dr. J. GREENWOOD WILSON (Cardiff) writes: The note in your issue of Nov. 11 (p. 636) says: "The Ministry of Health appointed a Central Housing Advisory Committee to make recommendations on the design, lay-out, construction, and equipment of dwellings." As this is not an accurate statement and does perhaps some injustice to the previous labours of the Central Housing Advisory Committee, will you permit me to explain the position more precisely. The Central Housing Advisory Committee was appointed by statute (Housing Act, 1935) to advise the Minister of Health on housing matters. Since its appointment the committee has in turn set up a number of subcommittees, all of which have done valuable work. Most of the recommendations of the subcommittees have been accepted, with or without modification, by the main committee, which in turn has passed them on to the Minister, and who, in turn, has usually accepted and acted upon the advice thus offered to him. The Central Housing Advisory Committee itself appointed a subcommittee, under the chairmanship of one of its distinguished members, the Earl of Dudley, to make recommendations on the design, lay-out, etc., of dwellings. Its report, known as the "Design of Dwellings" or the Dudley report, was published after it had been accepted by the Central Housing Advisory Committee, its parent committee, and in turn by the Minister of Health himself.

Sensitiveness to Strychnine

Dr. FRANK CROSBIE (Ealing, W.13) writes: One case in my practice endorses Dr. D. R. C. Shepherd's warning (Nov. 25, p. 694). Seven years ago I prescribed a mixture for a middle-aged married woman. She took one dose and promptly collapsed. I saw her within a few minutes; the symptoms, if severe, were fairly transitory. Four years later there was an exact repetition of this train of events. The one item common to both prescriptions was tinct. nucis vom. ♏ iv.

Tourniquets

Dr. J. L. BARFORD (Guildford) writes: On two or three separate occasions recently, when lecturing to mixed Army personnel, I have been astounded to be informed by members of the R.A.M.C. that they had been told that the latest instruction was that a tourniquet once applied should *never* be released. They were quite definite about this, and one—a very knowledgeable sergeant, R.A.M.C.—even murmured "histamine." I have tried in vain to ascertain at what school and by whom this iconoclastic instruction has been given. (See question and answer published Nov. 11, p. 648.)

Dyspareunia

Dr. S. H. WADDY (Huddersfield) writes: In reply to a query on dyspareunia (Nov. 11, p. 649) I note the crude, cruel, and embarrassing method of gradual vaginal dilatation is recommended for a young woman who is stated to be "rather highly strung and very apprehensive on examination." Surely this is the worst possible treatment and one calculated to make her loathe the thought of coitus, whether it be painful or not. I have a patient whose whole married life appears to have been spoiled by such treatment being carried out during her honeymoon in the South of England. She has had a child, but all sexual thought and action is abhorrent and the memory of the honeymoon a nightmare. As this method is not always successful, as suggested in the reply quoted above, why not carry out the far easier, quicker, more aesthetic, and more certain digital dilatation under nitrous oxide or intravenous anaesthesia, either on one's surgery couch or in the patient's own home? I have never yet found further dilatation necessary. The patient can be assured that her difficulty is over and she need have no further fear.

An Appeal Renewed

Owing to the need for severely restricting circulation of the *Journal* while the paper shortage lasts, a number of institutions and individuals connected with medicine and its ancillary services can no longer obtain the weekly copy for which they formerly subscribed. Any member who might be willing to pass on his *Journal* after reading it (making himself responsible for dispatch and postage) would be given the name and address of a suitable recipient if he wrote to the Publishing Manager at B.M.A. House, Tavistock Square, W.C.1. A substantial number of offers came in response to the appeal published on Aug. 26, but there is still a long waiting-list.